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ABSTRACT

This publication presents information for each of the 60 research projects active under the support of the Maternal and Child Health Research Program (MCHRP) in Fiscal Years 1990 and 1991. The variety of research topics and objectives pursued by the 60 investigations mirrors the broad mandate of the MCHRP as well as the eclectic and multidisciplinary approaches historically used by the Maternal and Child Health Bureau. The projects focus on applied research in the areas of medicine, health services, psychology, and epidemiology. The publication is divided into two sections--new and continuation projects. Information for each research project generally includes the grantee, investigator, project period, costs, statement of the problem, research questions or hypotheses, study design and methods, population description and sampling plan, analysis plan, and (for new projects only) pre-award evaluation information. A grantee index and project index conclude the document. (JDD)

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MATERNAL AND CHILD HEALTH RESEARCH PROGRAM

Active Projects FY 1990 and FY 1991

Maternal and Child Health Bureau
in conjunction with
National Center for Education
in Maternal and Child Health

EC 302437

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MATERNAL AND CHILD HEALTH RESEARCH PROGRAM

Active Projects FY 1990 and FY 1991

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TABLE OF CONTENTS

Preface vii

Program Activities ix

Maternal and Child Health Bureau Research Grants Review Committee Roster of Members—November 1991 xiii

New Grants Awarded 1

Perinatal Risks and Outcomes Among Low-Income Immigrants 3
Ruben G. Rumbaut, Ph.D. & John R. Weeks, Ph.D., San Diego State University

Iron Absorption by Infants 9
Samuel J. Fomon, M.D., University of Iowa

High-Tech Home Care for Children with Chronic Health Conditions 13
Juanita W. Fleming, Ph.D., University of Kentucky

Spouse Abuse and Pregnancy Outcomes: A Prediction Study 20
Gabriel Smilkstein, M.D., University of Louisville Research Foundation

Evaluation of the Guidelines for Maternal Transport 25
Donna M. Strobino, Ph.D., Johns Hopkins University

Behavioral and Familial Predictors of Injuries in Children 31
Penelope M. Keyl, Ph.D., Johns Hopkins University

State Census of Technology-Dependent Children 35
Judith S. Palfrey, M.D., Children's Hospital

A Parent-Focused Intervention to Reduce Pain During Procedures 40
Howard Bauchner, M.D., Trustees of Health and Hospitals of the City of Boston

Predicting Teenage Pregnancy 45
Joel W. Ager, Ph.D., Wayne State University

Feeding Method and Fat Tolerance in Very Low Birthweight Neonates 50
Seetha Shankaran, M.D., Wayne State University

Use of High Calcium Infant Formula to Prevent Plumbism 55
James D. Sargent, M.D., Dartmouth College

Predicting Preschool Function from Contingency Intervention 61
Michael Lewis, Ph.D. & Margaret W. Sullivan, Ph.D.
University of Medicine and Dentistry of New Jersey
Robert Wood Johnson Medical School

A Self-Management Educational Program for Severely Asthmatic Children 66
Shirley Murphy, M.D., University of New Mexico School of Medicine

Young Adult Users of Services for Children with Special Health Care Needs: Service Utilization, Psychological Status and Development Tasks 72
Henry T. Ireys, Ph.D., Johns Hopkins University

Improved Prenatal Detection of the Fragile X Syndrome 77
Edmund C. Jenkins, Ph.D. & W. Ted Brown, M.D., Ph.D.
Research Foundation for Mental Hygiene, Inc.

Effects at Age Five of an Intervention Program for Low Birthweight Infants 81
Cecelia M. McCarton, M.D., Albert Einstein College of Medicine

Body Composition in Pregnant Women 87
Sally Ann Lederman, Ph.D., Columbia University

Risk Detection Using Observations of Interaction 91
Julie A. Hofheimer, Ph.D., University of North Carolina at Chapel Hill

Otitis Media in Children and Later Language and Learning 96
Joanne Erwick Roberts, Ph.D., University of North Carolina at Chapel Hill

Fecal Coliforms and the Risk of Diarrhea in Child Care Centers 100
Jonathan B. Kotch, M.D., M.P.H., University of North Carolina at Chapel Hill

Psychosocial Sequelae of Bronchopulmonary Dysplasia and Very Low Birthweight 106
Lynn T. Singer, Ph.D., Case Western Reserve University

Single Parents and Early Intervention Programs: Participation and Goodness of Fit 110
C. Wayne Jones, Ph.D. & Donald G. Unger, Ph.D.
Philadelphia Child Guidance Center

Adolescent Mothering and Preschool Behavior Problems 116
Susan J. Spieker, Ph.D. & Robert J. McMahon, Ph.D., University of Washington

Drowning Prevention Through Swimming Lessons 121
Frederick P. Rivara, M.D., M.P.H., University of Washington

Continuation Grants 127

Health and Nutrition of U.S. Hispanic Children 129
Fernando S. Mendoza, M.D., M.P.H., Stanford University School of Medicine

Maternal Pesticide Exposure and Pregnancy Outcome 132
Winnie O. Willis, Sc.D., San Diego State University

Survey of Chronically Ill Children's Use of Time Out of School 136
Bonnie Holaday, R.N., D.N.S. & Anne Turner-Henson, R.N., D.S.N.
University of California at San Francisco

Risk-Taking Behavior in Adolescents: Impact of Puberty 140
Charles E. Irwin, Jr., M.D., University of California at San Francisco

Laboratory Evaluation of Jaundiced Newborns: A Reevaluation 143
Thomas B. Newman, M.D., M.P.H., University of California at San Francisco

Physiologic Risk Assessments to Predict Preterm Birth 146
Denise Main, M.D., California Pacific Medical Center

Evaluation of the Implementation of the Medi-Cal Comprehensive Perinatal Services .. 149
Carol C. Korenbrot, Ph.D., University of California at San Francisco

Effectiveness of an Urban Low Birthweight Intervention 153
Deborah L. Coates, Ph.D., The Better Babies Project, Inc.

Interaction and Support: Mothers and Deaf Infants 157
Kathryn Meadow-Orlans, Ph.D., Gallaudet University

Reducing the Nation's Pediatric Intensive Care Mortality 160
Murray M. Pollack, M.D., Children's National Medical Center

Identification of Risk for SIDS: Subsequent Siblings 163
Alfred Steinschneider, M.D., Ph.D.
American Sudden Infant Death Syndrome Institute

An Educational Behavioral Program for PKU 166
Kimberlee Michals, Ph.D., University of Illinois at Chicago

Nature, Origins, and Consequences of Conceptions of Parenting 169
Ronald L. Simmons, Ph.D., Iowa State University

Intravenous Antibiotic Therapy in Cystic Fibrosis: Home Versus Hospital 173
William W. Waring, M.D., Tulane University School of Medicine

Smoking Cessation/Relapse Prevention in Low-Income Mothers 176
Ruth R. Faden, Ph.D., M.P.H., Johns Hopkins University

Home Intervention for Infants with Failure to Thrive 179
Maureen Black, Ph.D., University of Maryland School of Medicine

Study of Psychosocial Factors in Maternal Phenylketonuria 183
Susan E. Waisbren, Ph.D., Boston Children's Hospital

Infants of Depressed Adolescent Mothers 186
Howard C. Bauchner, M.D., Boston City Hospital

Preconceptional Vitamin Use and Neural Tube Defects 188
Allen A. Mitchell, M.D., Trustees of Boston University

Coordinated Care and Case Management for Children with Special Health Needs 192
James M. Perrin, M.D., Massachusetts General Hospital

Early Intervention Collaborative Study: Preschool Phase 195
Jack P. Shonkoff, M.D., University of Massachusetts Medical School

Improving Memory in EMR Children 199
Hilary H. Ratner, Ph.D., Wayne State University

Outcome Evaluation of a Pediatric Health Care Model 203
Jack Elinson, Ph.D.
Medical and Health Research Association of New York City, Inc.

Determinants of Adverse Outcome Among Toddlers of Adolescent Mothers 206
Gail A. Wasserman, Ph.D., Research Foundation for Mental Hygiene, Inc.

A Multidimensional Health Status Index for Infants 211
Kenneth M. McConnochie, M.D., M.P.H.
University of Rochester School of Medicine and Dentistry

Study of Home Visitation for Mothers and Children 215
David L. Olds, Ph.D., University of Rochester Medical Center

Maternal Smoking and Vitamin/Antioxidant Status 220
Edward P. Norkus, Ph.D., Our Lady of Mercy Medical Center

Simultaneous Screening for Hearing, Speech, and Language 224
Raymond Sturner, M.D., Duke University Medical Center

Prediction of Outcome of Early Intervention in Failure to Thrive 227
Dennis Drotar, Ph.D., Case Western Reserve University

Otitis Media in Day Care: Effects on Language/Attention 230
Lynne V. Feagans, Ph.D., Pennsylvania State University

Behavioral Intervention with IUGR Infants 233
Cynthia Garcia Coll, Ph.D., Women and Infants Hospital of Rhode Island

Acculturation, Psychosocial Predictors, and Breastfeeding 236
David K. Rassin, Ph.D., University of Texas Medical Branch at Galveston

Uterine Activity Patterns: Definition with Home Monitor 238
Robert K. Creasy, M.D., University of Texas Health Science Center at Houston

Sickle Cell Anemia: DNA for Newborn Screening Followup 240
Edward R. B. McCabe, M.D., Ph.D., Baylor College of Medicine

Listening Partners: Psychosocial Competence and Prevention 243
Lynne A. Bond, Ph.D., University of Vermont

Epilepsy in Pregnancy: Developmental Followup of Infants 247
Mark S. Yerby, M.D., M.P.H., University of Washington

PREFACE

This publication presents information for each of the 60 research projects active under the support of the Maternal and Child Health Research Program (MCHRP) in FY 1990 and FY 1991. The information is presented in summary form similar to that used for a companion publication reporting on research completed in 1989, 1990, and 1991. A quick first reading of the summaries will reveal the variety of research topics and objectives pursued by the 60 investigations and the diversity of research traditions represented. Such variety mirrors the broad mandate of the MCHRP as well as the eclectic and multidisciplinary approaches that historically have been used by the Maternal and Child Health Bureau (MCHB) to carry out its mission. An underlying characteristic of the projects, as a group, is the applied nature of the research. This is consistent with the mandate contained in the amendment to Title V which established the research program in the early 1960's.

This publication is broadly divided into two sections—new and continuation projects. Within each of these two sections, projects are ordered according to grant number. The first two digits of the grant number represent the State where the grantee institution is located (i.e., MCJ-01 = Alabama). Thus, new and continuation projects are also arranged alphabetically according to State.

Except for the information in the pre-award evaluation, the content of the abstracts in the two sections is similar. The specific items of information contained within the summaries represent requests and suggestions from intended users of the inventory, both within and outside the Federal government. Many of these intended users are concerned with the development of discipline-specific knowledge and with the overall technical aspects of conducting research and interpreting research findings; hence, the preponderance of information on the research plan, particularly as it refers to research design, measurement approaches, sample size, and data analysis plan.

The information in the pre-award evaluation of projects is a synthesis of the written comments of the assigned reviewers and notes taken during the discussion that precedes the collective recommendation of the Maternal and Child Health Review Committee. There are several reasons why this information should be made available. First, it attests to the significance of the research questions and the technical quality of the research plan as judged by a panel of peers under a set of procedures that minimizes bias and promotes fairness and objectivity in the projects selected for funding. Second, the information in the pre-award evaluation indicates the strengths as well as the weaknesses of the proposal. This approach, it is felt, gives a more balanced view of the nature of funded research and emphasizes that, for the most part, it is always less than perfect. Third, the pre-award assessment information also attests to the contribution of the peer review process to the improvement of research that ultimately is funded. While the criticisms and suggestions for improvement made by reviewers are not binding on the investigators unless issued as conditions of the awards, they are usually attended to and adopted prior to conducting the research. Fourth, the information in the pre-award evaluation is instructive for those who practice or plan to practice the research crafts, particularly graduate students and new doctoral-level professionals seeking to establish a foothold in an extremely competitive field.

GONTRAN LAMBERTY, DR.P.H.
Director, MCH Research Program
May 1, 1993

PROGRAM ACTIVITIES

Program Description

The Maternal and Child Health Research Program (MCHRP) is authorized by Title V, Section 502 (a) (1) of the Social Security Act. The program is administered by the Division of Systems, Education and Science, Maternal and Child Health Bureau (MCHB), Health Resources and Services Administration (HRSA). HRSA is a component of the Public Health Service (PHS), part of the U.S. Department of Health and Human Services (DHHS). The purpose of the program is to support applied research relating to maternal and child health services which shows promise of substantial contribution to the advancement of such services. Findings from the research supported by the MCHRP are expected to have reasonable potential for transfer to health care delivery programs for mothers and children.

Other Federal entities are active in maternal and child health research. Foremost among them are the National Institute of Child Health and Human Development (NICHD), the National Center for Nursing Research (NCNR), the Agency for Health Care Policy and Research (AHCPR), and the National Institute for Mental Health (NIMH). Because of overlapping interests, these Federal agencies maintain close contact to ensure that duplication of efforts does not occur and that new areas of concern receive adequate attention. Frequently, funds are merged to support research that an individual entity might not be able to adequately fund independently, or that is of mutual interest. These joint ventures are identified in the Grant Award Information section of the project abstract.

Research projects are selected for support by the MCHRP using a peer review system similar to but independent of the NIH review system. The review group is called the Maternal and Child Health Bureau Research Grants Review Committee. It is composed of nongovernmental experts appointed for this purpose by the Secretary of Health and Human Services. Committee members are research scientists of national stature who are also experienced and knowledgeable in maternal and child health programs. They are selected from the fields of biostatistics, developmental psychology, epidemiology, nursing, nutrition, obstetrics, pediatrics, sociology, social work and public health. When the volume and/or content of the applications received for review require it, special and collateral reviewers are used to supplement the expertise of the Review Committee. Except for not voting, special reviewers participate in the review process in the same manner as appointed members of the committee. Collateral reviewers, on the other hand, submit their reviews by mail and do not otherwise participate or vote. The roster of reviewers active in November 1991 appears as the next section (*see* page xiii).

Review Results

Two hundred and fifteen (215) applications were reviewed by the program in FY 1990 and FY 1991 (*see* table 1). Fifty-two, or 24.2 percent, of these applications were non-competing (i.e., continuations) while the remaining 163, or 75.8 percent, were competing applications.

Of the 163 competing applications reviewed in FY 1990 and FY 1991, 159, or 97.5 percent, were "new," a category which includes applications submitted to the Research

Table 1. Number and Percent Distribution of Applications According to Recommendation: MCH Research Program FY 1990 and FY 1991.

Type of Application	Approved Applications	Disapproved Applications	Deferred Applications	All Applications
All Types	77 35.8%	136 63.3%	2 0.9%	215 100.0%
New	24 15.1%	133 83.6%	2 1.3%	159 100.0%
New-new	14 10.8%	115 88.5%	1 0.8%	130 100.0%
New-revised	10 34.5%	18 62.1%	1 3.4%	29 100.0%
Competing Extension	1 25.0%	3 75.0%	0 0.0%	4 100.0%
Continuation	52 100.0%	0 0.0%	0 0.0%	52 100.0%

Program for the first time, new applications from the previous cycle for which a recommendation for action was deferred by the committee, revisions of previously disapproved new applications, and revisions of previously approved applications that had remained unfunded because of an insufficient priority score. The rate of approval for the two subcategories of new applications differs considerably (*see* table 1). It was lowest for applications submitted for the first time (10.8 percent) and highest for revisions of previously disapproved applications (34.5 percent). The approval rate of 34.5 percent for the resubmission of previously disapproved applications reflects the conscious efforts of the committee to be constructive in their reviews as well as the willingness of disapproved applicants to respond to the criticisms and suggestions for improvement made by reviewers. In general, the "gross" approval rate of 15.1 percent (the number of new applications recommended for approval by the committee divided by the total number of new applications reviewed) is relatively low when compared to other Federal research programs such as those of the NIH. The "net" approval rate (the number of new applications actually funded, divided by the total number of applications reviewed) compares favorably with other Federal research programs, including NIH.

Unless there has been a significant departure from the originally approved project plan, a request for additional funds and/or evidence that the project is experiencing difficulties in execution, continuation applications are ordinarily reviewed by program staff and for the most part are assured of continuing support for the duration of the original approved project period.

Of all new applications accepted for review during FY 1990 and FY 1991, 34.0 percent address applied medical concerns, 31.4 percent address psychological concerns, 25.8 percent address health services, and 8.8 percent address epidemiological issues (*see* table 2). This distribution mirrors the Bureau's programmatic emphases on prevention, treatment, remediation, and problem definition.

Table 2. Number and Percent of New Applications by Type of Research: MCH Research Program FY 1990 and FY 1991.

Type of Research	Number	Percent
Total	159	100.0%
Medical	54	34.0%
Psychological	50	31.4%
Health Services	41	25.8%
Epidemiological	14	8.8%

Table 3. Number and Percent Distribution of New Applications According to Type of Research and Rates of Approval: MCH Research Program FY 1990 and FY 1991.

Type of Research	Approved	Disapproved & Deferred	Total
All Types	24 15.1%	135 84.9%	159 100.0%
Medical	12 22.2%	42 77.8%	54 100.0%
Psychological	5 10.0%	45 90.0%	50 100.0%
Health Services	5 12.2%	36 87.8%	41 100.0%
Epidemiological	2 14.3%	12 85.7%	14 100.0%

Applications addressing medical concerns had the highest approval rates (22.2 percent), followed by epidemiological concerns (14.3 percent), health services (12.2 percent), and psychological themes (10.0 percent) (*see* table 3). The low approval rate for applications addressing psychological themes may reflect the problems inherent in doing behavioral sciences research, which requires especially careful attention to measurement and study design considerations.

Active Projects

Of the sixty (60) research projects that were active during FY 1990 and/or FY 1991, 24 or 40.0 percent, represented new projects (*see* table 4). Forty-one percent of these new projects were revisions of applications previously reviewed and disapproved one, two or three times times by the MCHB Research Grants Review Committee.

One-third of the active projects (20 of 60) represent clinical and community interventions addressing, under clinical trial conditions, enduring maternal and child health problems such as reduction of low birthweight and infant mortality rates, coordinated care and case management for children with special health needs, early intervention for children with developmental vulnerabilities, preconceptional vitamin use

Table 4. Number and Percent Distribution of Active Projects According to Selected Characteristics: MCH Research Program FY 1990 and FY 1991.

Characteristics	Number	Percent
Total	60	100.0%
New	24	40.0%
Old	36	60.0%
Total	60	100.0%
Intervention	20	33.3%
Descriptive/ Correlational	40	66.7%

and neural tube defects. This high proportion of intervention research represented in the active projects indicates that the MCHRP is fulfilling the responsibility of developing new program components for the MCHB under high standards of scientific inquiry. The remaining 40 projects cover broad areas of maternal and child health concerns and represent future contributions that will expand the MCH scientific knowledge base.

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November 1991

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Associate Professor of Psychology
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NEW GRANTS

AWARDED

PERINATAL RISKS AND OUTCOMES AMONG LOW-INCOME IMMIGRANTS

GRANTEE San Diego State University

INVESTIGATOR
Ruben G. Rumbaut, Ph.D.
John R. Weeks, Ph.D.
Department of Sociology
San Diego, CA 92182
Telephone: (619) 594-5449 or 594-2874

PROJECT NUMBER MCJ-060595

PROJECT PERIOD 05/01/90–04/30/91

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	95,135	n/a	n/a	n/a	n/a
Requested	111,924	n/a	n/a	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

Recent research points to an apparent public health enigma among new immigrants to the United States: High-risk foreign-born groups, particularly low-income immigrants of Mexican and Southeast Asian origin, show unexpectedly favorable perinatal outcomes and seem to be "superior health achievers." To unravel the reasons for that finding, this study examines an extraordinarily in-depth data set drawn from the Comprehensive Perinatal Program (CPP) of the University of California at San Diego (UCSD) Medical Center.

From 1980 to 1991, when the program was suddenly phased out, the Comprehensive Perinatal Program provided a program of prenatal assessment, education, and health care to low-income women in San Diego County. Most of the pregnant women receiving CPP prenatal services and delivering their babies at the UCSD Medical Center were immigrants from Mexico, Vietnam, Laos, or Cambodia. The CPP data set consists of nearly 500 variables per case (including most of the variables listed in the research literature as likely determinants of pregnancy outcomes) for a large sample of both foreign-born and American-born women (including precisely those ethnic groups that are the focus of the investigation).

In the search for explanations of racial and ethnic differences in pregnancy outcomes, this study permits a multivariate analysis, in almost unprecedented detail, of biomedical and sociocultural maternal risk factors in their association with the immediate outcome of the pregnancy. Exactly how these factors combine with each other, and their relative causal role in shaping specific perinatal trajectories, is not yet known. The study's findings thus have significant theoretical and practical implications for health care policy.

Research Questions or Hypotheses

The study addresses four main research questions:

1. What ethnic and/or nativity differences exist among low-income women in their primary and secondary risk factors and perinatal outcomes?
2. What are the independent main effects of primary and secondary maternal risk factors and perinatal outcomes?
3. What significant interactions exist among the independent variables?
4. What risk factors, or combinations of risk factors, best explain the observed ethnic and/or nativity differences in perinatal outcomes?

These general research questions are addressed through a detailed analytical model from which specific hypotheses are derived for testing purposes. The model posits that perinatal outcomes (such as low birthweight, premature births, fetal and neonatal deaths) are influenced by the interaction of multiple risk factors (or determinants), conceptualized as primary or secondary, depending on how directly they impact on the fetus and on the pregnancy.

These risk factors are further distinguished analytically according to whether they are biomedical or sociocultural in nature. Biomedical factors include a wide range of characteristics that are specifically treatable by health care practitioners. Sociocultural factors include cultural background, socioeconomic status, social support, psychosocial stressors, and socially determined behavior (including substance abuse) that may alter the risks of poor reproductive outcomes.

Study Design and Methods

This research does not involve the actual collection of new data, but rather the abstracting, coding (in consultation with a staff physician), and computer entry of data already extant in Comprehensive Perinatal Program files. The CPP data consist of discrete medical, nutritional, and psychosocial assessments by a professional staff of physicians, nurse practitioners, licensed nutritionists, and psychosocial workers, yielding a data base of 476 independent variables per pregnancy.

Conventional clinical tests, performed by medical personnel, include physical and pelvic examinations, health (and previous pregnancy) history, anthropometry, and laboratory tests (blood tests, pap test, urinalysis, cervical culture). The measurement of specific nutritional intake, performed by a nutritionist through interviews with the expectant mother, is based on a 24-hour recall method. Also included is a dietary history and specification of substance abuse behaviors (smoking, alcohol, drugs).

The psychosocial assessment, based on interviews with the patient, uses a standardized check-off list to evaluate specific stressors, social support, and psychological state. (Detailed qualitative psychosocial progress reports are also available in CPP records for at-risk patients referred to a licensed social worker for intervention.) For non-English speaking mothers, the interviews are conducted with the help of trained bilingual/bicultural interpreters.

At the preliminary screening, demographic information is also collected (including education, occupation, income, household size, welfare eligibility, nativity and immigration status, language proficiency, and religion). The CPP data set in effect already controls for the fact that participating mothers share a common situation of economic disadvantage (to be eligible they must meet low-income criteria), as well as the same type of prenatal care services and the same hospital setting for delivery. Although the CPP data have been gathered since the program's inception, no analysis has ever been undertaken prior to the present study.

In addition to the wide range of information on maternal risk factors collected by the program, CPP records document maternal data on all deliveries at the UCSD Medical Center, including medical diagnoses and information on complications of pregnancy, labor, and delivery.

From separate hospital records, an infant outcome form is developed for each baby delivered at the medical center, providing a variety of outcome measures (or dependent variables), including birthweight, gestational age, head circumference, Coombs' index, VDRL reaction, Apgar scores, diagnoses at birth, complications, and length of hospitalization of the baby. All of these infant outcome variables are coded and entered into computer files, and then matched with the mothers' data files to produce a final comprehensive data set for analysis and hypothesis testing.

Population Description and Sampling Plan

Data were collected for all eligible low-income women receiving prenatal services through the CPP program, and for all of their babies delivered at the UCSD Medical Center, for the two most recent fiscal years (1989–1991). Most but not all of these women deliver at the UCSD Medical Center; some may deliver at other hospitals in the San Diego metropolitan area, and a smaller number may move out of the region prior to delivery. As a result, complete 1989–91 maternal data were collected for 2,320 pregnancies, of which 1,464 records included matched hospital outcome data for their babies delivered at the UCSD Medical Center.

In addition, maternal data from CPP records were collected for another 1,004 pregnancies occurring during the two previous fiscal years (1987–89). The total sample of data on mothers thus consists of 3,324 cases. However, given the focus of the study on the effect of maternal risk factors on perinatal outcomes, the core of the analysis is limited to the 1,464 records for which complete maternal and infant outcome data are available. The final sample thus reflects the characteristics of all women receiving CPP prenatal services and delivering at the UCSD Medical Center (the principal hospital providing health care services to the indigent in San Diego County) during 1989–91.

The sample is broken down by nativity and ethnicity into native-born and foreign-born African American, Anglo, Asian, and Hispanic women. The first two groups consist primarily of women born in the United States; the latter two groups consist primarily of immigrants. Of the 1,464 women included in the data set to be analyzed, 253 (17 percent) were born in the United States, and the remaining 1,211 (83 percent) were born outside the United States, predominantly in Latin America or Asia. Of the foreign-born Hispanic women, 88 percent were born in Mexico, and nearly all the rest in Central America; of the foreign-born Asian women, 68 percent were born in Vietnam, Laos, or Cambodia, and nearly all the rest in the Philippines, Korea, Taiwan, or China.

Analysis Plan

The analysis focuses on the identification of those factors, or combinations of factors, that best distinguish the perinatal outcomes of several different subgroups, broken down by nativity and ethnicity: American-born and foreign-born women of African American, Anglo, Asian, and Hispanic origin. It consists of a systematic test of hypotheses drawn from the conceptual framework described above. Because of the large number of variables (nearly 500 in total), the process begins with a factor analysis to reduce the number of independent variables (risk factors) to a workable size. The independent variables are then examined separately to see if nativity and/or race and ethnicity account for the observed variability with respect to the independent variables. Correlations and interactions among the independent variables are then examined in order to establish the most plausible mix of independent variables suggested by the conceptual framework as having a potential influence on pregnancy outcomes.

Pregnancy outcomes (dependent variables) are examined individually to see the extent to which the set of independent variables explains their variability, looking especially at the extent to which nativity and race/ethnicity may play a role in explaining the outcomes under investigation. The outcomes are then scaled to provide an overall quantitative outcome index, scored from 0 (perinatal death) to 1 (optimal outcome reflecting no perinatal complication), which provides the final test of the conceptual model.

Data analysis relies throughout on appropriate multivariate techniques. Thus, a series of analyses of variance are performed to assess between-group differences in perinatal outcome for each set of independent variables. This allows identification of those risk factors which are significant indicators of group differences, for entry into more complex regression models.

To test the conceptual model, logistic regression analyses are performed. The results of the logistic regression are compared with an analogous analysis of least-squares multiple regression. The analysis concludes with an examination of qualitative data drawn especially from the detailed psychosocial reports. These pieces of information are used to shed further light on the quantitative findings derived from the statistical analysis.

PRE-AWARD EVALUATION

Originality and Importance

This proposal builds on the findings recently reported by these investigators of lower infant mortality rates among Mexican-American and Indochinese refugees (especially Vietnamese and Cambodian) in San Diego. The principal investigators plan to use detailed medical, sociodemographic, nutritional, and behavioral data available from a large comprehensive perinatal program to seek to identify health promoting, as well as health diminishing, activities. Although the specific variables to be studied are not unique, these investigators plan to use the data in a new way (i.e., by identifying health promoting activities in well-defined ethnic subgroups).

Regional and National Significance

This study could provide useful ethnic-specific data which would be of particular value in California, but could probably be extrapolated to other Mexican American and Indochinese populations throughout the United States. Its potential significance is reduced by the inability to include a comparable subsample of American blacks, a sizeable proportion of whom are at abnormally high risk for an unfavorable pregnancy outcome, but even here it would provide a model for specific hypothesis testing with regard to various factors or combinations of factors which statistically contribute to either positive or negative pregnancy outcomes in this important minority group.

Scientific and Technical Merit

This proposal, a resubmission of a proposal that was previously disapproved, is very carefully developed and presented. The problem is presented in a clear and convincing manner, and is readily researchable, using existing data. The investigators do a convincing job of justifying the importance of the study and pointing out the practical applications it could have with respect to formulating policies and developing intervention programs to enhance the probability of favorable pregnancy outcomes among high-risk groups.

The review of the literature is basically confined to recent research on the maternal and child health status of Southeast Asians, but it is sufficient to establish a clear rationale for the study proposed here. In addition, it presents a concise review of the various factors known to be related to pregnancy outcome, and it organizes and summarizes them in terms of a general conceptual framework which then serves as the basis for the study design and analysis plan.

Four principal research questions that are directly related to the problem as stated are listed as a guide to the research. In addition, a detailed analytical model is presented—one that is derived from the preceding conceptual model and which lists the many independent variables by conceptual category and the outcome morbidity and mortality dependent variables. No hypotheses are offered here, but they could easily be derived from the model; and later in the proposal, in the discussion of data analysis plans, the investigators illustrate how specific hypotheses will, in fact, be derived from the model for testing purposes.

The proposal does raise some concerns. First, risk factors are classified somewhat arbitrarily as primary (i.e., directly affecting perinatal outcome) versus secondary. It might be more appropriate, for example, to include prepregnancy weight for height and weight gain in the primary group. Although stress and psychological factors are clearly of interest to this research team, they may not be viewed by other investigators as established, clearly-linked risk factors. Given the carefully designed, multiple approaches to analysis, however, actual categorization as primary or secondary should be less important.

Second, it is critical to be assured that the data set to be used is actually complete. How often were psychosocial and nutritional assessments not performed on patients or lost? Did the forms remain stable from 1980 to 1989? How well defined is perinatal outcome in these outpatient charts (i.e., are complete delivery records included, or perhaps poorly legible notes)? It will obviously require more time if the hospital chart also needs to be reviewed to determine length of stay, delivery complications, and accurate gestational age.

Third, what safeguards will be employed to study accuracy of data abstraction and entry? How will inconsistencies in charted information be coded (i.e., differences in parity, substance abuse, birthweight, etc.)?

Fourth, the investigators plan to use individual pregnancies rather than individual women as the analysis unit. They believe this approach to be appropriate as long as fewer than 5 percent of the pregnancies are to the same women in the sample. Given the 9-year study period, the fact that this program was the primary source of patient care for indigent women, the propensity of a woman to return for subsequent care to the same provider, high fecundity, and the low socioeconomic status of the sample, many more repeat pregnancies would be anticipated in the sample. Should a way be selected to choose only one representative pregnancy for each individual prior to extensive abstraction?

Fifth, this work may take more time to complete and require more data abstraction than requested by the investigators.

Approval is recommended, pending assurance of adequacy of information that has already been collected.

IRON ABSORPTION BY INFANTS

GRANTEE University of Iowa

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PROJECT NUMBER MCJ-190606

PROJECT PERIOD 7/1/91–6/30/94

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	207,280	176,187	193,805	n/a	n/a
Requested	205,829	228,006	250,809	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

Iron deficiency is the most prevalent nutritional deficiency of infants and small children in the United States. It seems probable that iron deficiency of preschool children is most commonly a consequence of inadequate absorption of iron during the first year of life. Iron stores present at birth are inadequate to meet the needs for iron incorporation into the rapidly expanding hemoglobin mass and myoglobin mass, and the dietary conditions that apply to a substantial portion of the infant population result in too little iron absorption to meet the need. Developing strategies to prevent iron deficiency is particularly urgent because of the large body of evidence suggesting that iron deficiency in infants and preschool children interferes with cognitive development.

Using the least abundant stable (nonradioactive) isotope of iron, ^{58}Fe, as a tracer, this project studies erythrocyte incorporation of iron (which is closely related to but somewhat less than iron absorption) from iron-fortified infant formula and from iron-fortified foods that are commercially available now or are attractive candidates for future iron fortification.

Research Questions or Hypotheses

Question 1: Is there a significant difference in absorption of iron (mg/day) from formulas fortified at the level of 12 mg of iron per liter, compared to formulas fortified at 8 mg of iron per liter? Iron inhibits absorption of certain other minerals. Therefore, if iron absorption is similar from formulas fortified with 8 and 12 mg of iron per liter, fortification at a level of 8 mg per liter would be preferable.

Question 2: What is the extent of non-heme iron absorption from the following two iron-fortified beikost: (a) Rice cereal fortified with ferrous fumarate, and (b) strained beef and vegetables?

Study Design and Methods

Standardized conditions of study are used to determine in normal iron-sufficient infants the extent of iron absorption as reflected by erythrocyte incorporation of iron from test feedings. Venous or capillary blood is obtained from the infants at 112, 140, 168, and 196 days of age, and analyzed for hemoglobin, hematocrit, mean corpuscular volume, serum iron, transferrin, erythrocyte protoporphyrin, ferritin, and the mass isotope ratio between ^{58}Fe and ^{57}Fe ($MIR_{58/57}$). The $MIR_{58/57}$ values at 112 and 140 days of age serve as baseline, and the extent of enrichment of erythrocytes with ^{58}Fe is calculated from the $MIR_{58/57}$ values at 168 and 196 days of age.

Question 1: From 112 to 196 days of age, infants in Group 1 are fed a milk-based formula providing 12 mg of iron per liter, and infants in Group 2 are fed the same formula, except the level of iron fortification is 8 mg per liter. At 154 days of age, a precisely weighed amount (about 1 mg) of a solution of ^{58}Fe-enriched ferrous sulfate (providing approximately 0.4 mg of iron and 0.3 mg of ^{58}Fe) is added to 480 ml of the formula and consumed by the infant in two feedings under supervision in the Pediatric Metabolic Unit. During the remainder of the 24 hours, formula that is not labeled with ^{58}Fe is consumed, and the quantity consumed is determined by weighing the containers. This regimen is repeated at 155 and 156 days of age.

Question 2: Beginning at 112 days of age, the infants are fed a milk-based formula providing approximately 2 mg of iron per liter. At 140 days of age, a food similar to that scheduled as the test meal is introduced and fed at least once daily. The test meal is fed in the Pediatric Metabolic Unit once daily at 154, 155, and 156 days of age. Test meals are fed midmorning, 2 hours after a formula feeding and 2 hours before the next formula feeding. The iron fortified foods are: (a) Powdered rice cereal fortified with ferrous fumarate (48 mg of iron per 100 g of dry cereal—7 mg/100 g after dilution); and (b) strained beef with vegetables fortified with ferrous sulfate (7 mg of iron per 100 g). Each of the three test meals includes 0.3 mg of ^{58}Fe.

Population Description and Sampling Plan

Normal-term infants are recruited at 112 days of age, upon completion of other studies in our unit. Equal numbers of male and female infants are included in each study. There are no restrictions regarding race.

Question 1: Based on an estimated coefficient of variation of 30 percent, a study of 32 subjects in each group will permit us to detect a difference of 0.75 standard deviations with a power of 0.9 (one-tailed *t* test). We therefore plan to enroll 37 infants in each group to allow for a dropout rate of 15 percent.

Question 2: We want to determine whether mean erythrocyte incorporation of iron from the ferrous fumarate-enriched rice cereal or the ferrous fumarate-fortified beef with vegetables is 3.5 percent of intake or greater (3.5 percent incorporation is believed sufficient to motivate manufacturers to explore marketing of the products). Using Stein's two-stage sample size estimation with an estimated coefficient of variation of 40 percent, 18 subjects (9 males and 9 females) in each group will provide a 95 percent confidence interval for erythrocyte incorporation of ^{58}Fe of 3.5–5.5 percent of intake.

Analysis Plan

The quantity of administered ^{58}Fe incorporated into erythrocytes ($^{58}Fe_{inc}$) at a specified time after administration of the dose. Statistical comparison of cohorts in the various feeding studies (iron-fortified formula or beikost) utilizes analysis of variance for factorial designs. When appropriate, erythrocyte incorporation data is transformed (using logarithms) for analysis, and geometric means are reported. Covariance analysis is used when adjustment for serum ferritin is desired.

PRE-AWARD EVALUATION

Originality and Importance

This is an innovative and elegantly designed classic study that is extraordinarily important to the welfare of almost all infants and preschool children in the United States. Strategies for meeting the iron needs of infants and preschool children have been difficult to develop because little information is available regarding iron absorption. Developing strategies to prevent iron deficiency is particularly urgent since considerable new evidence suggests that iron deficiency interferes with performance on tests of mental development, and that these effects may be lasting. The systematic study of iron absorption with ^{58}Fe tracers in infants will provide the essential data needed to develop these strategies. Data from this study will open a new vista in our understanding of iron absorption. In addition, the results have the potential to markedly alter fortification of foods, feeding practices, and recommendations for all older infants and preschool children.

Regional and National Significance

This study has significance for almost all infants born each year in the United States (approximately 4 million) and for millions of preschool children.

The principal investigator convincingly argues for the envisioned application of the study. These investigators are pioneers in infant nutrition and the study of iron absorption. They have developed (and published) the state-of-the-art tracer methodology essential for this study and, furthermore, synthesized the heme iron that contains the intrinsic tracer label. Iron absorption in infants is researchable with this newly developed methodology.

Scientific and Technical Merit

The proposal is carefully and thoughtfully prepared. The literature review is logically organized and provides a plausible theoretical framework for the objectives of the study. The investigators provide preliminary data for each of the three questions that support the scientific rationale and document their critical thinking and ability to successfully complete the study.

The three questions to be answered are clearly stated, testable, and logically derived from the preliminary data and literature review. The proposal is elegantly designed, conceptually simple, and profound in its relevance to understanding basic concepts of iron nutrition as well as the practical issues related to feeding of older infants. The forms of iron to be studied and the levels of enrichment of formula/biekost are reasonable and appropriate. This information would be directly applicable to infant feeding.

Food consumption data are not essential for the data analysis (details for determining food consumption are not provided); however, careful monitoring of food consumption to maintain constant conditions is a strength of the study. These investigators have been completing classic infant studies for more than 20 years, using meticulous techniques for determining food consumption. The statistical procedures are detailed and appear appropriate.

The investigator will obtain data from groups of infants as homogeneous as possible with respect to age, iron nutritional status, and circumstances of the study; thus, these data will not be representative of all infants in the United States. Nevertheless, this study will provide valuable data. The population will be carefully selected: Normal-term iron-sufficient infants who are within ±4 days of the specific age will be entered into the study. Infants who have a serum ferritin concentration considered low (<20 mg/ml, approximately 5 percent of the infants) will be excluded.

Approximately 34–40 term infants recruited from Iowa City and the surrounding community will be studied each year. This will provide an adequate number of infants for the study, including additional infants to allow for reasonable attrition rates of 10–20 percent. These investigators have a long-term success rate in recruiting infants and maintaining rapport with families; this is evident from their success in followup enrollment of children at 8 years of age (469 of 471 were located), and from the fact that, in many cases, more than one infant from the same family has participated in the study.

The time schedule is realistic. Demonstration of satisfactory absorption of iron from cereals fortified with ferrous fumarate (question 2a) will be completed first, in less than 1 year; the study of infant formulas (question 1) will be completed during the second year; and the studies of non-heme iron-fortified vegetable/beef and heme iron-fortified beef will be completed in the third year.

HIGH-TECH HOME CARE FOR CHILDREN WITH CHRONIC HEALTH CONDITIONS

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PROJECT NUMBER	MCJ-210577
PROJECT PERIOD	10/01/89–09/30/91

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	340,147	96,954	n/a	n/a	n/a
Requested	228,287	87,263	n/a	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

The aim of this study is to create a data base that will aid in further describing technology-dependent children being cared for in their homes.

The objectives of the study are to:

1. Identify selected demographic characteristics of technology-dependent children cared for at home, and of their families;
2. Define home care of technology-dependent children in terms of consumption of resources;
3. Test selected hypotheses regarding the effects of home care of technology-dependent children on their families; and
4. Provide a means for these data to be used by others in developing recommendations for nursing practice in relation to the care of technology-dependent children and their families in home settings.

Research Questions and Hypotheses

This study tests the following hypotheses:

1. There will be a difference in the family level of stress among the families of ventilator-dependent children, children receiving intravenous therapy, children with daily dependence on specific support devices, and children requiring monitoring of vital functions.
2. There will be a difference in the impact on the family among the families of ventilator-dependent children, children receiving intravenous therapy, children

with daily dependence on specific support devices, and children requiring monitoring of vital functions.

3. There will be a difference in the adaptive behavior among ventilator-dependent children, children receiving intravenous therapy, children with daily dependence on specific support devices, and children requiring monitoring of vital functions.
4. There will be a difference in the social support of the family among the families of ventilator-dependent children, children receiving intravenous therapy, children with daily dependence on specific support devices, and children requiring monitoring of vital functions.
5. There will be a difference in the level of the caregiver's depression among the families of ventilator-dependent children, children receiving intravenous therapy, children with daily dependence on specific support devices, and children requiring monitoring of vital functions.
6. There will be a difference in the level of caregiver satisfaction among the families of ventilator-dependent children, children receiving intravenous therapy, children with daily dependence on specific support devices, and children requiring monitoring of vital functions.
7. The type of dependency affects family stress level, impact on the family, child's adaptive behavior level, and the amount of social support, which in turn determine the caregiver's level of depression and level of satisfaction.

Study Design and Methods

This study will provide both descriptive data and information from the testing of a number of relevant hypotheses. Large cities in different census regions of the United States are used to obtain data from families receiving services from both public and private agencies that serve technology-dependent children in their homes. Parents are interviewed by telephone and asked to respond to specific questions. Mothers are interviewed when possible, since they usually are the primary caregivers.

All families selected for the survey receive an introductory letter stating the general purpose of the study, the method of selecting the family, and the type of questions that will be asked; the letter explains that participation is voluntary, data will be kept confidential, and all identifying information will be destroyed at the end of the study. The letter also states that $10 will be provided to respondents who complete the interview, in appreciation for their time. For individuals who agree to participate but do not have a telephone, arrangements are made for telephone access for the interview.

Providing information in the introductory letter about some of the types of questions that will be asked is designed to help families with recall. Standardization of some of the time periods in the interview guide will also help to facilitate recall. To validate some of the data obtained from families, random checks are made concerning types of services offered by agencies in general, but not specific services used by individual study participants.

Population Description and Sampling Plan

The sample consists of a broad representation of parents of technology-dependent children in the United States. Subjects are parents of technology-dependent children ranging in age from 1 month to 19 years. The age range of the participating parents is broad and covers the years usually associated with child care. Parents of children in the finite stage of care or receiving hospice care are not included in the study. A total of 1,040 families of children who are technology dependent and who have been cared for in the home for at least 1 month are selected.

A purposive approach is used to select the sample. Sites are selected in four major regions of the country; all agencies involved in providing home care to technology-dependent children in these regions are then contacted and agency personnel are asked to create a list of all families with technology-dependent children who are being cared for at home. This list constitutes the sampling frame for the study in each city. A total of 80 families are sampled from this list in each of the 13 cities included in the study. The definition and classification of technology-dependent children employed in the Office of Technology Assessment (OTA) study (1986) is used in this research. The sample drawn from each city is stratified so that one-half of the families sampled have children who need monitoring of vital functions (OTA study type 4). The remaining half are families with children who are ventilator dependent, require intravenous nutrition or drugs, or require intensive monitoring (OTA study types 1, 2, and 3). This stratification plan has been developed with the recognition that there are at least four times as many children who need monitoring of vital functions (type 4) as there are types 1, 2, and 3 combined.

To avoid the problem of agencies providing only the names of persons they wish to include in the study, every effort is made to obtain a nonbiased sample. All agencies involved in providing home care to technology-dependent children are contacted. Hospitals as well as agencies that may serve these children (such as respite centers) are included. Individuals who know of parents who may have technology-dependent children are also contacted.

Analysis Plan

Data from the surveys are edited, coded, and then computerized. Since the Survey Research Center has a very reliable system of hand-editing individual items on the survey, the editing portion of the computerized data emphasizes consistency checks between related items on the survey. A computer program is being written to make the consistency checking as efficient as possible.

Data analysis then proceeds in two phases: Descriptive statistics and hypothesis testing. In the first phase, simple descriptive statistics are constructed to summarize the responses to each survey item. In addition, cross-tabulations are constructed between pairs of response items on the survey. Of particular interest are those tabulations that allow us to establish patterns in the nursing and economic resources consumed by the dependent child (objective 2). To meet this objective, we describe the number of nursing visits required (per unit of time), their average length, the care provided during these visits, their cost, and the payment source. We also describe how consumption of these resources varies with the etiologic variables: Type of dependency, length of time with the dependency, and length of time in home care. We also describe how consumption of these resources varies with the demographic variables: City of residence; age, race, and sex of the child; and family structure (objective 1).

Finally, we consider the results of the analysis for hypothesis testing and assess the extent to which resource consumption varies by type of dependency and the most relevant social and psychological variables, such as social support.

Each of the nine subscales of the Family Inventory of Life Events (FILE) is measured on an interval scale, and these subscales are most likely correlated. In the second phase of the data analysis, to determine whether the mean profile of the nine subscales varies with the type of dependency of the child, a multivariate analysis of variance (MANOVA) procedure is used. This procedure relies on a multivariate normal distribution assumption for the nine subscales in homogeneous subsets (in this case, each level of dependency) and a common covariance matrix for the nine subscales between the various levels of dependency. Each of these assumptions is verified by using various procedures in the Statistical Analysis System (SAS) package before proceeding with the analysis. If we can further assume that the common covariance matrix satisfies the Hunyh-Feldt structure, then this MANOVA can be replaced by an analysis of variance (ANOVA) procedure for the repeated measures experiment. This assumption may be verified by using the repeated measures option on the general linear models procedure in SAS.

Several additional analyses are performed to test the first hypothesis. As the children are sampled, they are stratified into two major strata: (1) Children requiring only monitoring of vital functions, and (2) children requiring either intravenous therapy or a ventilator or a specific support devise. We sample approximately 40 children from each of these two groups in each of the 13 cities. In testing hypothesis 1, it is also of interest to poststratify the second group into the three subgroups. According to the OTA report, the number of children in these subgroups most likely will not be equal. To adjust for these unequal group sizes, an appropriate multiple comparisons procedure such as the Tukey-Kramer method is used to make pairwise comparisons between the group mean levels of any subscale of the FILE.

A second consideration in testing the first hypothesis is that even after poststratification, children having the same level of dependency could still constitute a very diverse group of subjects due to various demographic and etiologic variables such as socioeconomic status, city of residence, duration of condition, type of agency administering home care, etc. Hence, a statistical analysis which accounts for these covariates will be investigated. This will be achieved through a regression analysis framework for a multivariate response variable.

A similar analysis strategy is undertaken when investigating the effect of type of dependency on the four dimensions of family impact (hypothesis 2), the four domains of the child's adaptive behavior (hypothesis 3), the dimensions of social support (hypothesis 4), the level of depression of the child's caregiver (hypothesis 5), and the level of satisfaction of the child's caregiver (hypothesis 6). The analysis for the dependent variables (satisfaction and depression) are considerably simpler, since each of these variables is measured in one dimension (i.e., the MANOVAs reduce to a simple ANOVA and the multivariate regression reduces to a simple multiple regression model or analysis of covariance).

To test hypothesis 7, a similar but separate analysis is conducted for each of the dependent variables (depression and satisfaction). The approach to testing this hypothesis for each variable is outlined below for the level of depression of the caregiver as measured by the Center of Epidemiologic Studies Depression Scale (CES-D). A structural equation model is fitted to our conceptual schema for hypothesis testing, in which the covariates are treated as an exogenous variable while family stress (nine indicators), family impact (four indicators), child's adaptive behavior (four domains), and family social support are intervening variables for the dependent variable, depression. To determine the effect of the type of dependency on this schema, separate structural equations models are fitted for each group of children: Ventilator-dependent, intravenous-dependent, specific support device-dependent, and those requiring only monitoring of vital functions. These causal models may then be compared between these four groups. Since level of depression as measured by the CES-D is known to be a highly skewed dependent variable, an analysis based on a logarithmic transformation of the dependent variable will be investigated.

Finally, since our conceptual schema is only a working model, other versions of this model are fitted to these data to determine the interrelationship between the exogenous, intervening, and dependent variables.

PRE-AWARD EVALUATION

Originality and Importance

The proposed research is original and important to maternal and child health. The use of complicated technology in home care for children can be expected to increase and there seems to be little research that specifically addresses the issues raised in this project, particularly relative to nursing practice in the home and consumption of resources by these technology-dependent children and their families. While the number of such children may be small (less than 1 percent of the population of children), they use an estimated 25–40 percent of total health care dollars and services.

Regional and National Significance

The proposed sampling design makes this a study which has both regional and national importance. The focus is on children in large cities representing a broad geographical area, which is a reasonable way to study the questions that are posed. A strength of the study could be the ability to compare results among major census regions. If successful, the study would have both regional and national significance since it would provide new information about technology-dependent families and children being cared for in their homes throughout the United States.

Scientific and Technical Merit

This application is a modification and resubmission of a proposal that was earlier reviewed and disapproved. The present application represents a significant change in study design compared with the previous proposal. This has resulted in a substantial budget reduction. The investigator has provided a cover letter outlining her responses to each of five concerns raised. The most significant change is that telephone interviewing will now be used exclusively, rather than the previously proposed face-to-face interviewing. This change accounts in large part for the reduction in budget. The more modest specific aim (objective 4) is an improvement made in response to the previous review. Overall, the merits of the proposed study are that it will result in more information on numbers of patients, costs, type of care, nursing practices, and resource consumption for technology-dependent children and their families. This is not an incidence or prevalence study, and is not presented as one. Because of the defined sampling scheme, new information on the demographics of these families will become available, and should be useful information. The possibility of sampling biases is recognized by the investigator. Generally, the goals and objectives are achievable, and the hypotheses are testable.

The proposed research is complementary to the 1986 OTA study, which focused on identifying technology-dependent children. The Vanderbilt Study (1986) addresses policy matters, which are not of primary interest to this investigator's research, so there is no overlap there, either. The use of the OTA definition and classification of technology-dependent children in the present study seems to be a meritorious approach. The selection of census regions and cities within their subregions is appropriate. The proposed sampling scheme is reasonably detailed. The use of liaison/consultants is essential to the successful completion of the study. The data analysis plan is adequate, and in some respects, quite sophisticated. Clearly, there has been input from knowledgeable statisticians.

The feasibility of this study continues to be a concern. Can we be assured that the appropriate agencies will provide high quality, complete lists of the families that are eligible for the study? There is an impressive set of letters (although a year old) from liaison/consultants and others indicating their support and cooperation. The fact still remains that the agencies themselves may not wish to make available the necessary information. The application still fails to address this issue satisfactorily.

Very little, if any, progress on the pilot study and final survey questionnaire has been made since the previous submission. While this is understandable, a serious concern with the presently proposed telephone interview is the length of time that will be needed to gather all the information. Can the test instruments be satisfactorily administered over the phone? How much time is needed? Will complete, valid, and reliable information be obtained? Use of well-trained interviewers is a plus, but some convincing pilot data need to be presented before funding for the entire study is provided.

There is no mention of whether some of the questionnaires will be available for visual reference at the time of the telephone call. For scales such as the FILE, the Family Impact Scale, the Personal Resource Questionnaire, the CES-D, and the Vineland Social Maturity Scale, this might be a strategy to streamline the interviewing session and produce more reliable responses.

A poorly justified change in the application relates to creation of a data tape for use by others. Doing this properly is not a trivial task. The content and usefulness of the tape are dependent on the quality of the information gathered. If the data are of high quality, it seems that the data should be analyzed, summarized, and published by the investigators, rather than leaving it to others. Therefore, this task should be deleted, as no strong evidence of interest in such a tape has been provided. Publication of the methodology and results in a peer-reviewed journal should be the goal by the end of the second year of funding.

This application is an improvement over the earlier one. Concerns still remain, however, particularly with respect to obtaining the required sample size and the instrument development. The recommendation is for approval, with the condition that the investigator show evidence that the required sample size is obtainable.

SPOUSE ABUSE AND PREGNANCY OUTCOMES: A PREDICTION STUDY

GRANTEE University of Louisville Research Foundation

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PROJECT NUMBER MCJ-210600

PROJECT PERIOD 10/01/90–09/30/93

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	115,904	116,787	105,107	n/a	n/a
Requested	116,691	132,967	126,506	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

Few studies exist that relate spouse abuse to pregnancy outcome; yet, spouse abuse is a life stressor that has been identified in as many as 11 percent of pregnant women. As a life stressor, spouse abuse represents a psychosocial risk that may adversely influence pregnancy outcome. Thus, pregnancy outcome problems such as prematurity, low birthweight, and low pediatric Apgar scores (which have been identified as consequences of psychosocial risk) may be expected with spouse abuse. Premature and term low birthweight infants represent a major health problem. There is a great need for studies that will identify causes of low birthweight, for the consequences are high perinatal morbidity, increased postnatal hospital care, high infant morbidity and mortality, and impaired intellectual and motor performance.

This study pays special attention to social support as a modifying variable. The knowledge gained from such a study will facilitate implementation of more effective alerting systems to identify gravidas at high risk for compromised infant outcomes. From reported studies on spouse abuse during pregnancy, there appears to be a need for research that has the following components: (1) A validated instrument for identification of the physically abused woman; (2) a clear timeline delineating the time of the abuse; (3) a demographic profile documenting socioeconomic status; (4) identification of the abuser and knowledge of those living in the household; and (5) documentation of lifestyle factors, psychosocial resources and stressors, and biomedical risk. This study has been designed to respond to these needs.

Research Questions or Hypotheses

The study hypotheses address the relationship of biomedical, psychosocial, lifestyle, and spouse abuse factors to complications at delivery, including low birthweight, prematurity, pediatric Apgar scores (at 1 and 5 minutes), and prolonged labor.

Hypothesis 1: A history of physical abuse during the pregnancy will result in increased incidence of maternal complications at delivery and poorer infant outcomes.

Hypothesis 2: Delivery complications will be related to biomedical risk, impaired social support, depression, lower self-esteem, and external locus of control.

Hypothesis 3: Abused gravidas who perceive the social support of family and/or friends to be available and of high quality will have more favorable pregnancy outcomes than abused gravidas who perceive their social support to be low.

Study Design and Methods

This study is a prospective cohort design, using matched samples of obstetric patients. The study prospectively evaluates the influence of spouse abuse—alone, and in combination with psychosocial and biomedical risk factors known to influence pregnancy outcomes. It is a 3-year longitudinal study that follows two matched groups of women. One group consists of those who perceive themselves as having been abused during their pregnancy by a spouse/partner or other family member. The second group consists of a matched group of pregnant women who have not been abused. All subjects who identify themselves as having been abused are seen by the project's social worker or graduate research assistants. To meet the project's ethical and legal responsibilities, a woman who identifies herself as having been abused is told of the reporting requirement and given an opportunity to talk with a member of the State spouse abuse unit via telephone immediately. At this time, the woman may refuse services and no further reporting is required.

Alternatively, she may elect to have her name submitted on a weekly form to be contacted by letter at a later time. At time of contact, she may either accept or reject the offer of aid. There is no legal ramification for the abuser under this law. All of the women are given educational materials and advised of services available at the Spouse Abuse Center in Louisville, as a part of the regular intake interview. Women who are potential subjects are then informed of the study and asked to participate. Informed consent is explained and participants are asked to sign consent forms. In final patient interviews after delivery, subjects are asked whether they (1) used the resources of the Spouse Abuse Center or other social services, and (2) experienced abuse during the study period.

Spouse-abused patients are identified (or eliminated) for group membership based on their response to a global screening statement and their definition of the abuse as having occurred during the current pregnancy. A positive response at any point in the study, including the final question at delivery, places the subject in the spouse-abused (SA) group. Similarly, continual denial of spouse abuse makes the subject eligible for membership in the non-spouse-abused (NSA) group.

Population Description and Sampling Plan

The study groups consist of 400 spouse-abused women and 400 non-spouse-abused women and are formed by group-matched sampling of women who use the services of the prenatal clinic in the Department of Obstetrics and Gynecology, University of Louisville School of Medicine. Subjects are matched for age, race, marital status, parity, education, lifestyle factors (smoking, drinking, drug use), and gravidity. A positive match requires the following factors: Age (±2 years), race, marital status, gravidity, parity, and at least two of the other four factors. Only black women and white women are included, since mothers in these two racial groups comprise 99 percent of all deliveries (35 percent of the patients are black women, 64 percent are white). Currently, women who deliver at Humana Hospital at the University of Louisville are, on average, 22 years of age, 27 percent are primagravida, and 60 percent are para < 2. These characteristics are replicated in the sample to ensure that it is representative of the hospital population.

The difficulty with requiring such a complex sampling frame is the potential for too few subjects for matching and, thus, empty cells in the design. However, due to the large sample size and the hospital population characteristics described previously, we believe that appropriate matching subjects can be located. Subjects are followed in the clinic in the usual manner, throughout the course of their pregnancies. Clinic patients rarely fail to continue with prenatal care once they have begun, so dropouts are unlikely. Should patients be lost to followup, comparisons will be made of initial variables between completers and dropouts to determine whether some systematic bias is operating.

Analysis Plan

This project requires a number of data analytic tasks. Descriptive analyses of the distribution shapes, ranges, and central tendencies of variables are conducted and reported to establish suitability for later analyses. Correlational analyses to highlight patterns of interrelationships among variables to be statistically controlled are also analyzed. Finally, multivariate analyses directed toward actual hypothesis testing are also conducted.

Since the methods of descriptive and correlational analyses are well known, we focus on the analysis strategy leading to actual hypothesis and model testing. The first stage of this study involves developing statistically based scoring strategies for the instruments. The second stage uses these scores in actual model and hypothesis testing.

The task of the second stage is to derive models that predict pregnancy outcomes (birthweight, prematurity, Apgar scores at 1 and 5 minutes, and uterine dysfunction) from knowledge of group membership (spouse-abused or non-spouse-abused)—alone and in combination with psychosocial factors and biomedical risk, including demographic and lifestyle factors. Because of the multivariate nature of this task, logistic and multiple regression are the two primary analytic techniques. Both techniques permit evaluation of the contribution of one variable, while statistically controlling for the effects of other variables. In addition, both techniques allow assessment of the effect of cross-product or interaction terms on the outcome. Thus, the interaction of group membership with other variables can be analyzed. The general model tested takes the following form: Biomedical Outcome (e.g., birthweight) = b_1 (control factors) + b_2 (group membership)

+ b_3 (biomedical risk) + b_4 (psychosocial stressors) + b_5 (psychosocial resources) + b_6 (social resources) + $b_{7\text{-}k}$ (selected interactions), where the "b" values are empirically derived regression weights and the descriptors in parenthesis describe variable categories. The "$b_{7\text{-}k}$" term represents potential interaction terms (e.g., group membership × social resources) analyses that determine differential prediction of the outcome variables for subsets of the predictor variables.

PRE-AWARD EVALUATION

Originality and Importance

Estimates of the occurrence of spouse abuse during pregnancy vary, but as many as 10 percent of all pregnant women may have been subjected to abuse. Despite this, little research has been conducted on the effects of spouse abuse on pregnancy outcomes. Such research is needed to assess the risks to pregnant women and their children and to aid in the development of intervention programs for women at risk.

Regional and National Significance

The problem of spouse abuse is not limited by geographical area. Although spouse abuse has been reported more frequently in women with low socioeconomic status, this may reflect reporting biases rather than actual differences in incidence. As there is no description of the population to be studied in this proposal, it is difficult to determine how representative the sample will be of the larger population of abused women.

Scientific and Technical Merit

This is a revision of a previously reviewed proposal to extend the principal investigator's research on a biopsychosocial model in relation to health behaviors to a new domain, spouse abuse. In the previous round of reviews, the Review Committee agreed that this proposal had a number of strengths. The literature review compellingly demonstrates that abuse is a significant problem for women, especially during pregnancy. The concepts and hypotheses are clearly stated, and the biopsychosocial model offers a comprehensive framework for assessing the effects of abuse on pregnancy outcomes. The proposed measures are documented and are, for the most part, valid, reliable, and well-known. The data analysis strategy is appropriate, although the analyses are not specified in great detail (the procedures for selecting appropriate interaction terms are not specified, nor have the control variables been defined).

Nevertheless, a number of problems, primarily having to do with subject selection and measurement, were identified. These concerns have been addressed in the following ways in this revision.

First, there were concerns about recruitment and confidentiality, and the principal investigator was encouraged to do a small feasibility or pilot study to address these issues. The principal investigator states in his letter to the Review Committee that preliminary studies conducted over the past year indicate that women will answer questions related to spouse abuse if they are provided with a safe environment as part of the usual intake screening. Unfortunately, more information about such a pilot study was not included in the resubmitted proposal. The procedures for ensuring confidentiality while satisfying legal reporting requirements are now described in detail and appear adequate: If women respond positively to questions about spouse abuse during the intake interview, they will be told about State reporting requirements, and they will be offered an opportunity to talk with the State spouse abuse unit. Women will be informed that they may refuse the unit's services at that time, and no further reporting will be necessary. They may also choose to have their names given to the unit in a weekly report for later contact, but they may refuse services at a later date as well.

The principal investigator has also specified more carefully the procedure for defining spouse abuse. In this revision, only women who have been abused during the current pregnancy (as opposed to having been abused sometime in the past) will be included in the study group. Women who have been abused in the past (but not during the current pregnancy) will be considered eligible for the control group. The principal investigator might consider comparing women who have never been abused by their spouses with women who have been abused in the past but not during the current pregnancy. However, since the focus of this project is on pregnancy outcomes, the control group as currently defined is appropriate.

This revision also clarifies that initial screening will be done only for women who present for prenatal care before their third trimester. Women can enter the study group at any time during their pregnancy, however, if they respond affirmatively to questions about abuse.

Additional variables have been added to the sampling frame, as requested. It is now proposed that subjects in the control group be matched on age (± 2 years), parity, education, and lifestyle factors, in addition to the previously defined variables of race, gravida, and marital status. A positive match will require age, race, gravidity, parity, marital status, and at least two of the other four factors. This is an important refinement, since previous research suggests the importance of these variables.

The principal investigator addressed the criticisms of the neonatal outcome measures, as specified in the previous proposal, by providing some evidence that the measures chosen are appropriate. No changes in outcome measures were made. Furthermore, questions about measurement of newborn maturity and gestational age were addressed: Maturity will be assessed according to the Dubowitz scores, and gestational age will be assessed by a variety of indices. Finally, in response to criticisms, the budget has been reduced by 19 percent. These modifications have significantly strengthened the proposal.

EVALUATION OF THE GUIDELINES FOR MATERNAL TRANSPORT

GRANTEE	Johns Hopkins University
INVESTIGATOR	Donna M. Strobino, Ph.D. School of Hygiene and Public Health Department of Maternal and Child Health 624 North Broadway Baltimore, MD 21205 Telephone: (301) 550-5451
PROJECT NUMBER	MCJ-240586
PROJECT PERIOD	10/01/89–09/30/92

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	195,395	229,654	179,733	n/a	n/a
Requested	195,396	251,856	178,644	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

This study is designed to evaluate the guidelines for transfer of high-risk mothers from community hospitals to perinatal centers, using data from a sample of women admitted for labor and delivery in the hospitals that comprise the Southern New Jersey Perinatal Cooperative (SNJPC). Developing regionalized systems for delivery of perinatal care has been a major accomplishment during the past two decades. An important component of these systems is the transport of women with complicated pregnancies from community hospitals to tertiary centers. Most previous research on maternal transport has compared the morbidity of infants born to women who were transported before delivery with the morbidity of newborns transported after birth. No large population-based study has evaluated the outcomes of high-risk mothers who were transported before birth with the outcomes of high-risk mothers who remained in community hospitals.

Research Questions or Hypotheses

This study specifically addresses two hypotheses: (1) Transferring pregnant women to a tertiary center conforms with the guidelines for transport recommended by the American College of Obstetricians and Gynecologists, the American Academy of Pediatrics, and the March of Dimes; and (2) transferring pregnant women to a tertiary center is optimal when their newborns are expected to develop complications requiring intensive care because the technology needed to manage high-risk infants is available immediately after birth.

Study Design and Methods

This study is a nonconcurrent prospective study. It is prospective in following mothers from the prenatal period until delivery and following infants from birth to hospital discharge (or death), using medical records; and through the first year of life, using vital records. The design is nonconcurrent since data for the study are obtained from medical records for births in the SNJPC hospitals in 1984 and 1985. There are four sources of data for the study. Medical records from the 15 SNJPC hospitals and Philadelphia and Wilmington hospitals receiving maternal and neonatal transports provide the major source of data. Detailed clinical data are abstracted from medical records about the prenatal, intrapartum, and postpartum course of the mother and the nursery stay of the newborn. Separate data abstraction forms are used for the referral and receiving hospitals when mothers or newborns are transported. Data on any important events during transport are recorded on a transport form.

The second source of data for the study consists of labor and delivery and nursery logs maintained at all SNJPC hospitals. These logs are used to select the study sample. Linked birth and death records for all births in the seven counties in southern New Jersey are the third source of data. These data are linked with the medical records data and are used to measure mortality during the first year of life. The final source of data consists of questionnaires completed in 1980 and 1985 by SNJPC hospitals for certification of level of hospital. Both sets of questionnaires, which include information about available equipment and staff as well as staffing ratios and nursery size, are the source of the data describing hospital characteristics.

The study focuses on both the process and the outcome of maternal transport. The dependent variable for the study of the process of transport is the likelihood of transport, defined by a dichotomous variable indicating whether a mother was transported. It becomes the major independent variable in the analysis of outcome of transport. Outcome of transport is evaluated for both the newborn and the mother. Newborn outcomes include: 5-minute Apgar scores, length of nursery stay, duration of assisted ventilation, duration of oxygen therapy, presence and severity of respiratory distress syndrome, confirmed neonatal sepsis, seizures, intraventricular hemorrhage, necrotizing enterocolitis, and infant mortality. Maternal outcomes include length of postpartum hospital stay, maternal postpartum infection, and presence of significant postpartum morbidity, as measured by renal failure, congestive heart failure, persistent hypertension, excessive hemorrhage, and change in mental status.

Independent variables include obstetric and medical complications, demographic characteristics, and hospital characteristics. Complications studied include premature rupture of membranes, preterm labor, maternal hypertension, multiple gestation, third trimester bleeding, diabetes, heart disease, other chronic disease, isoimmunization, and maternal infection. When feasible, level of severity of illness is assessed for these variables. Demographic characteristics include maternal age, race, parity, marital status, source of payment for care, number of prior preterm births, number of prior fetal losses, and adequacy of prenatal care. Hospital characteristics include level of hospital, distance from nearest tertiary center, size of nursery, and capability to manage intermediate ventilatory support for the newborn. In addition, several feasibility-of-transport variables are studied: Condition of the mother and length of labor at time of admission, availability of beds at tertiary centers, and consultation on transport. Two potential confounding variables, caesarean delivery and birthweight of the newborn, are included in the analysis of maternal and newborn outcomes.

Population Description and Sampling Plan

The study is population-based, including all high-risk transported and nontransported mothers (and their newborns) who were admitted for labor and delivery at the 15 SNJPC hospitals in 1984 and part of 1985. The study mothers or their newborns may have been transported to SNJPC hospitals or to several hospitals in Philadelphia and Wilmington. The SNJPC is a nonprofit network of the hospitals that provide maternal and newborn care in the seven southernmost counties in New Jersey. In 1981, the network was designated and certified as a demonstration joint Level III perinatal center with regional perinatal services provided at Our Lady of Lourdes Medical Center and Cooper Hospital University Medical Center. Since 1984, the SNJPC has been the primary organizational structure coordinating perinatal services and activities in southern New Jersey.

The study sample includes all women transported from SNJPC hospitals in 1984 and the first half of 1985, and all women transported from Level I hospitals in the second half of 1985. Nontransported women are sampled from all hospitals in 1984, as well as from Level I hospitals for the first 6 months of 1985 and from Level II and III hospitals for the first 3 months of 1985. Eligibility criteria for the study, based on guidelines for maternal transport, include gestation of less than 36 weeks, birthweight of 2,000 grams or less, or one of the following complications: Placenta previa, abruptio placentae, pregnancy-induced hypertension, insulin-dependent diabetes, heart disease, other underlying chronic disease, trauma, and drug use. Study subjects are identified through elaborate labor and delivery and nursery logs maintained at all SNJPC hospitals.

The study sample includes 137 transported and 337 nontransported women from Level I hospitals, 173 transported and 697 nontransported women from Level II hospitals, and 539 nontransported women who delivered at the Level III SNJPC hospitals. Fifty-one of the transported women were transferred to Pennsylvania hospitals. The study sample also includes 215 infants (born to study participants) who were transported after birth.

This study is an extension of earlier research conducted in the SNJPC hospitals and funded by the National Center for Health Services Research. Data were collected in this research on many sample subjects who delivered in SNJPC hospitals during 1984 and on their newborns; however, the sample was not sufficiently large to evaluate the impact of interhospital transport. The present study extends this previous study by collecting additional data on a sample of high-risk women for 1985 (176 transported and 472 nontransported women) and a sample of women who delivered in the SNJPC tertiary hospitals (approximately 290 women). In addition, data are collected on approximately 50 mothers and 160 newborns who were transported to hospitals in Philadelphia and Wilmington.

Analysis Plan

Analysis of the data focuses first on the determinants of maternal transport, with special interest in the extent to which the determinants conform to established guidelines for transport. Logistic regression analyses are used to investigate the variables associated with maternal transport in a multivariate framework. Variables in this analysis include: Maternal complications, their severity, and gestation of presentation; maternal demographic variables; feasibility of transport variables; and hospital characteristics.

As a second step in the analysis, pregnancy outcomes for transported and nontransported mothers are compared, as are outcomes for transported mothers and control mothers who delivered in SNJPC tertiary hospitals. These comparisons are made for specific complications, severity of complications, and (where numbers permit) level of hospital. A multiple regression analysis is performed to evaluate the relationship of maternal transport to maternal and newborn outcomes, adjusting for complications, demographic variables, feasibility of transport variables, and birthweight. Logistic regression is used for the dichotomous dependent variables; multiple linear regression is used for the continuous dependent variables. All analyses are conducted on aggregated individual and hospital data so that no individual or hospital can be identified.

PRE-AWARD EVALUATION

Originality and Importance

Little research has been devoted to the extent to which transfer of maternal high-risk patients is applied uniformly, or the impact of transfer on maternal and neonatal outcomes. This study is exciting because it is the first to address these issues with a large population-based sample.

Regional and National Significance

Transfer of maternal high-risk patients is a keystone of regionalized care. Information derived from the study could have a major impact on health care delivery practice.

Scientific and Technical Merit

This is an extremely detailed proposal in which hypotheses are carefully presented and amply justified. The review of the literature is complete and state-of-the-art. A strength of the proposal is that it builds on the principal investigator's recent work, which was funded to develop a measure of the need for transport of high-risk mothers and newborns from community hospitals to tertiary centers. An additional strength relates to the use of an index of severity previously developed. The development and rationale of this index is carefully described in the present proposal. The index seems to be analogous to a relative risk measure. With the expertise of two local perinatologists, three thresholds will be selected for the index in this study: One that maximizes sensitivity, one that balances sensitivity and specificity, and one that maximizes specificity. The investigators will evaluate the value that yields the best results in terms of outcomes.

Other strengths of this proposal are the clearly presented data sources and data abstraction plans included in the appendix. Quality of data and abstraction will be monitored to assure accuracy and completeness.

However, there are problems with this proposal. First, the investigators imply that guidelines for maternal transport are well established and widely accepted. In Appendix A, however, the guidelines they present are often vaguely defined and not categorized by level of referring hospital.

The second concern relates to the choice of dependent and independent variables. There are seven dependent variables to define newborn health status: (1) Neonatal morbidity, defined by a continuous variable of the number of neonatal risk factors with a score of 5 or 10 included in the Hobel neonatal risk score; (2) neonatal morbidity rate, defined as a dichotomous variable equal to 1 if the newborn had 3 or more risk factors in the Hobel neonatal risk score, and zero otherwise; (3) infant mortality rate, a dichotomous variable defining death within the first year of life; (4) neonatal mortality rate, a variable defining death within the first 28 days of life; (5) neonatal mortality for the first day, defined as death in the first 24 hours of life; (6) neonatal mortality in the first 2 days, defined as death in the first 48 hours of life; and (7) neonatal mortality in the first 7 days, defined as death within the first 7 days of life. It is of concern that neonatal morbidity is linked only to the 1973 Hobel score. While this score was state-of-the-art 15 years ago, it does not include many of the major neonatal complications now seen, such as respiratory distress requiring ventilatory support, necrotizing enterocolitis, intraventricular hemorrhages, or patent ductus arteriosus. Furthermore, prematurity is defined only as birthweight of less than 2,000 grams, with no additional subgroupings for lower birthweights or earlier gestational ages. It appears that more current morbidity information related to morbidity of much smaller babies would be of greater value. The mortality data, while defined in traditional ways, is unlikely to be very illuminating, given this relatively small sample size (albeit of high-risk infants).

Two other dependent variables in the study are related to maternal postpartum health status: (1) Length of maternal postpartum hospital stay, defined as a continuous variable in total number of days; and (2) obstetric or medical intensive care, a dichotomous variable defined by admission or nonadmission to such a unit. However, the proposal does not define specific characteristics that constitute these intensive care units or the specific postpartum morbidity that occurs.

The definition of a large percentage of the study's independent variables, particularly the medical variables, is also a concern. These key variables are designed to assess type and severity of maternal complications. Many are defined not by standard obstetric criteria but, rather, by more unusual criteria, presumably arrived at by the investigators. For example, the definition of idiopathic premature labor is labor begun before 34 weeks' gestation without prenatal or intrapartum complications necessitating delivery; however, no information is provided regarding cervical dilatation, effacement, or use of tocolytic agents.

Maternal hypertension is defined on a scale of one to four (where zero equals none): (1) Pregnancy-induced hypertension, mild toxemia, or mild pre-eclampsia; (2) chronic hypertension; (3) pre-eclampsia, moderate or severe toxemia; and (4) eclampsia.

These are to be based on the clinician's diagnosis in the record. As a more quantitative assessment of severity of maternal hypertension, the investigators seek to define it with the following scale (zero equals none): (1) Elevated blood pressure but no protein or other symptoms; (2) elevated blood pressure and protein but no other symptoms; (3) elevated blood pressure or protein in urine with evidence of oliguria, or reduced platelet counts; and (4) seizures with other evidence of eclampsia. These definitions take into account neither the degree of hypertension, nor the degree of proteinuria, nor other potential complications of pre-eclampsia. The American College of Obstetricians and Gynecologists has a standard definition of mild, moderate, and severe pre-eclampsia that would be much more useful than this self-derived scoring system.

Similarly, maternal diabetes severity is defined as a continuous variable using the following scale (zero equals none): (1) Prediabetes, gestational diabetes (noninsulin-dependent); (2) gestational diabetes (insulin dependent); (3) diet controlled; (4) insulin-dependent diabetes, well controlled; and (5) insulin-dependent diabetes, poorly controlled. It is not clear how the data abstractors are going to decide on level of control. It appears that the investigators would do better to use standard White criteria to define diabetic severity, with additional clearly defined criteria to assess level of control.

There are additional concerns with a large number of the other medical variables. Additional independent variables include summary prenatal risk scores and intrapartum risk scores based on the 1973 Hobel risk scoring system. This is a relatively old score and is only moderately predictive at best.

The data analysis plan is described in reasonable detail. It will use descriptive and chi-square analyses, followed by a logistic regression analysis. However, some of the analyses are slightly questionable (e.g., use of a *t* test to compare differences in the regression coefficients between two regressions). The analytic methods, while probably appropriate if used carefully, seem to be somewhat superficially described, with too much of an exploratory data analysis plan. This is probably a function of the large number of hypotheses to be tested. Nevertheless, the principal investigator seems organized enough for the data analysis to proceed successfully and thus yield useful results.

BEHAVIORAL AND FAMILIAL PREDICTORS OF INJURIES IN CHILDREN

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PROJECT NUMBER MCJ-240591

PROJECT PERIOD 11/01/89–04/30/93

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	255,650	242,225	290,537	122,233	n/a
Requested	251,062	288,425	339,484	158,203	n/a

* Indirect included

SUMMARY

Statement of the Problem

This study addresses the important public health problem of childhood injuries by investigating the association of child behavior, family structure, and environment with injuries among school-age children in Baltimore. During the past 50 years, the importance of childhood injuries as a public health problem has been recognized increasingly, as the impact of infectious diseases has declined. The cost of injuries in terms of medical care and rehabilitation costs, the lost potential, and the permanent disabilities that remain make injuries one of the most expensive health problems today.

Previous research focusing on the role of child behavior and family structure in predicting childhood injuries has been primarily retrospective in design. This study uses a prospective, longitudinal design to study the relationship of child behavior and family structure and functioning to injury liability. Findings from this study will be useful in designing successful interventions to reduce a child's injury liability.

Although gender and racial differences are not a primary focus of this research, these issues can be addressed with the data obtained. The sample is drawn from five ethnically and socioeconomically diverse areas in east Baltimore, making it feasible to examine the impact of ethnic variations on the relationship of child and family factors to injury liability.

Research Questions or Hypotheses

This study addresses six hypotheses:

1. Injury liability is increased for children who exhibit aggression, hyperactivity, risk taking, anxiety, or lack of concentration;
2. The relationship of injury liability to aggression, hyperactivity, risk taking, anxiety, and lack of concentration is strengthened if the behavior is severe, persistent (stable over time), or pervasive (noted in more than one context);
3. There is no effect of depressive affect or social isolation on injury liability;
4. There is synergy in the effect of co-occurrence of child behavior and psychological characteristics on injury liability;
5. There is no independent effect of family structure or socioeconomic status on injury liability, net of family functioning; and
6. Injury liability is increased for children living in families characterized by conflict, loose controls, little cohesion, disorganization, poor child supervision, or extremes of discipline practices (very lenient or very strict).

Study Design and Methods

This study employs a concurrent prospective design. The parent or primary caretaker and the child are interviewed annually. Data are collected on child behavior, family structure, family functioning, household composition, and the physical characteristics of the home environment. Data on child behavior include information on the child's participation in sports and leisure activities and completion of the Child Behavior Checklist (CBCL). The CBCL allows for the assessment of aggressive, delinquent, depressive, and hyperactive behavior. Measurements of family functioning include the Family Environment Scale and a scale to assess family conflict resolution style. Measures of parent discipline and monitoring are also included, and the child's motor coordination is assessed.

Data on injury events are collected at 6-month intervals and include information on the type of injury, sequence of events leading to the injury, and medical services required to treat the injury. In addition to spontaneous reports of injuries, the primary caretaker is asked about different situations in which an injury might have occurred and about different types of injuries the child might have experienced, as a way to stimulate the caretaker's memory of forgotten injury events.

Population Description and Sampling Plan

The study sample is drawn from a cohort of children who began first grade in the fall of 1985. These children have been studied as part of an ongoing longitudinal intervention trial through the Prevention Research Center (PRC) of the Department of Mental Hygiene at The Johns Hopkins School of Hygiene and Public Health and the Baltimore City Public School System. The goal of the intervention trial is to reduce later behavior problems among the intervention participants. The children in the intervention trial attended 19 different schools in Baltimore, and were drawn from 5 urban areas that varied by ethnicity, housing, family structure, and income.

The inclusion criteria for the injury study are as follows: (1) The children attended 1 of the 19 PRC schools in first or second grade and entered first grade in academic year

1985–86; (2) data were obtained by PRC from the children and their teachers at least twice between the first and third grades; (3) parent interviews were completed by PRC during the 1988–89 academic year; and (4) children resided in Baltimore and attended a Baltimore city public school in the 1989–90 academic year.

A total of 710 children were identified as eligible for the first injury interview, conducted in the spring of 1990. At that time, the average age of the children was 10.8 years. Approximately 90 percent of the sample has been followed over the subsequent 2 years of followup.

Analysis Plan

During preliminary analyses, the relationship of child behavior and family factors to injury liability is explored. For the purpose of these bivariate analyses, the dependent variable, injury liability, is conceptualized as (1) the probability of experiencing an injury during the first and second years of followup, and (2) the number of injuries experienced during the first and second years of followup. Chi-square tests are used to test for the unadjusted relationship of the independent variables to injury liability.

The first stage of multivariate analyses includes a series of logit analyses to determine the relationship of the independent variables measured at one point in time to the risk of injury over the subsequent period of time. These multivariate analyses permit the determination of the independent effect of each independent variable after adjusting for the effects of background demographic factors and the other independent variables. Examining the importance of the pervasiveness of behavioral factors requires the measurement of behavior in multiple settings. Data are available on child behavior from three sources: Parent report, child report, and teacher report (from PRC data). Multivariate logit models are developed to determine the relationship of multiple reports of behavioral problems to injury liability.

Examining the importance of the persistence of child behavioral and family functioning factors requires the use of a longitudinal analysis strategy. A longitudinal logit model will be developed using recently developed statistical methodology that takes into account the correlation between observations over time.

PRE-AWARD EVALUATION

Originality and Importance

Childhood injuries are a major health concern, and an area that is in great need of systematic research. The principal investigator clearly details these issues in the proposal. While there have been a number of attempts in the past to explore issues related to childhood injuries, many of these investigations have been methodologically inadequate. This proposal incorporates a number of novel ideas, along with an important prospective research strategy. Particularly impressive is the clear conceptual rationale for the investigation provided by the principal investigator, and the integration of developmental constructs such as reciprocity and transactional processes in the formulation of factors which may prove predictive of childhood injuries.

Regional and National Significance

The study is being conducted in Baltimore, but the problem of childhood injuries clearly is a national one. Results from this study have the potential for national significance, as the population is a diverse one from a large urban area.

Scientific and Technical Merit

This is a meritorious proposal in numerous respects. The principal investigator has an excellent grasp of the area and the issues involved, and has presented them clearly. A strong rationale is provided for the work and for the chosen research design. In many ways, this proposed investigation builds on previous research which has been conducted in the area, and has the advantage of integrating an important project with an ongoing longitudinal study related in important conceptual ways. The ability to use and add to the data collected by the PRC study is a real strength, and will offer the ability to investigate prospective behavioral and family characteristics which might be predictive of childhood injury.

Another advantage is that the sample is collected and available from these earlier PRC data collection periods, and many of the sample characteristics are already known. The measures collected by the PRC and available to this project are certainly appropriate to the issues involved and should prove quite valuable. In addition, the measures that will be collected solely as a function of the proposed project seem appropriate and interesting, although there are questions as to the quality of data some might provide (e.g., children's perceptions of parental supervision).

Although this is a strong proposal, there are some areas of concern. One issue involves the double-edged sword of integrating this research with that of the PRC study. The advantages of this arrangement are discussed above, but several disadvantages are clear as well. First, there is the question of whether an intervention study provides an appropriate sample and context in which to conduct a descriptive study of injuries. Some discussion of how the interventions might affect the injury status of the children needs to be presented; the issue of how intervention group membership will be handled in the data analysis needs greater attention. Combining the groups to conduct analyses may be problematic—one would hypothesize that group differences in injury rates should be found if the interventions were successful and the principal investigator's theory holds true. Furthermore, what control and access will the principal investigator have in relation to the measures and their use? Since a number of the investigators from the PRC study are listed as personnel on this grant as well, perhaps that will not be a problem. However, the issue of how data will be shared needs to be more clearly described.

The plan for data analysis is not as clearly explained as one would hope. One specific issue involves the lack of clear relationships between the hypotheses presented and the data analysis plan to address these hypotheses. It is not clear how the major questions of this research protocol will be treated specifically in the analyses, and which analyses are planned for which questions. This is clearly a project rich in data, with the ability to address a number of critically important theoretical and practical issues in relation to the predictors of childhood injury. It is critical, therefore, to clearly describe the goals and feasibility of data analyses.

STATE CENSUS OF TECHNOLOGY-DEPENDENT CHILDREN

GRANTEE Children's Hospital

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PROJECT NUMBER MCJ-250590

PROJECT PERIOD 10/01/89–09/30/91

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	136,609	165,815	n/a	n/a	n/a
Requested	156,699	144,560	n/a	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

Advances in medical and surgical technology in the last 20 years, as well as new material development, miniaturization, and recognition that clean techniques can often replace sterile procedures, have led to a new reliance by physicians and surgeons on long-term technologic care for patients. These new practices have brought both new opportunities and new challenges. On the one hand, the new technologies have enhanced the life span of many patients and increased their chances to lead more functional lives. On the other, there have been greatly increased needs for long-term nursing, rehabilitation, and support services for this population of individuals who are dependent on medical technology and have complex medical needs.

In order to plan effective strategies for providing the services needed by children assisted by medical technology, it is essential to have a grasp of the size and configuration of the population to be served. In 1987, our research group (Project School Care) carried out a project to delineate the characteristics of the population of children in Massachusetts who were assisted by medical technology. This gave a one-time, cross-sectional look at the population, but did not give any appreciation of whether the population was increasing in size, nor the rate of increase (if any).

The purpose of the current investigation is to obtain a second data point in a similar manner to the data obtained in 1987, in order to assess longitudinal trends in the prevalence of technology dependence among children. By obtaining a comparable data set, questions regarding the size of the population, background characteristics, and parameters of medical technology use can be explored. Thus, we can estimate resource needs in communities, as well as some early delineations of trends. We recognize that having one additional data point will give only the direction of the movement, not the magnitude, but we feel this is important to document.

Research Questions or Hypotheses

This study has four specific aims:

1. Estimate the number of children in Massachusetts who are dependent on medical technology as of March 1990;
2. Estimate trends in the size of the medically dependent population by comparing data collected in the original 1987 study with data collected in 1990;
3. Use 1990 census data to estimate the prevalence of medical dependence by age; and
4. Determine the extent to which children depending on medical technology are living and attending school in the community.

Study Design and Methods

The study is a 1-month point prevalence census of all children depending on medical technology in Massachusetts in March 1990. The original census instrument was developed in 1986 and used in March 1987. In order to compare data from 1987 to 1990, the same census instrument (with only modest modifications) and the same study methods are used.

All pediatric, nursing, and educational providers likely to have contact with children assisted by medical technology are alerted to the census effort by mailing. This includes the medical and nursing directors of all hospitals with pediatric beds, nursing homes, pediatricians, Department of Public Health case managers, school nursing and special education directors, and directors of programs such as early intervention, multidistrict collaborative organizations, and the Massachusetts Association of 766 Approved Private Schools (MAAPS). The providers fill out an individual census form on each child known to them.

We hoped there would be redundancy in responses on children in the census so that we could estimate a standard error of response and be assured of the reliability of our data gathering effort. As a result, we made sure to ask for census information from all service sectors.

Once the data are available, they are coded and entered into the computer, and a sorting procedure is used to look for duplicate cases based on background characteristics (initials, age, gender, zip code). From this sorting procedure, unique data sets are derived, representing unique individuals. In the case of multiple census responses, to increase reliability of information, algorithms are used to prioritize educational responses from educational personnel and medical information from medical informants.

Population Description and Sampling Plan

The study is designed to determine the number of children in Massachusetts in 1987 and 1990 who depend daily on medical technology, including tracheostomy, respirators, oxygen, suctioning, nasogastric tubes, gastrostomies, jejunostomies, ileostomies, colostomies, urostomies, clean intermittent catheterization, intravenous lines or devices, and dialysis. Since the goal of the study is to describe a sample of children chronically dependent on medical technology, the sample is limited to children ages 3 months to 18 years, in order not to bias the sample with neonatal intensive care unit residents who may be temporarily technology dependent. All children are residents of Massachusetts.

Analysis Plan

This study employs a capture-recapture census method for estimating the size of a closed population. Capture-recapture census data are used to estimate the number of individuals in mobile populations or in populations that cannot be isolated and counted at one particular point in time. The technique was originally developed to estimate the number of fish in fisheries and animals in forests; in recent years, it has been applied to human populations as well. The technical idea behind a capture-recapture census is as follows: Two attempts are made to identify every member of the target population. This information is then used to create two lists of the target population. A two-way contingency table is created, displaying the number of individuals on both lists, those on list one but not on list two, and those on list two but not on list one. The following figure demonstrates how a contingency table works:

		List One		
		Yes	No	Total
List	Yes	a	b	$a+b$
Two	No	c	d	$c+d$
	Total:	$a+c$	$b+d$	$a+b+c+d=N$

The best estimate of the size of the total population is the sum of the four entries: $a+b+c+d=N$. However, only three entries are known: (a), (b), and (c). The last cell (d) is unknown because it represents the people missed by both lists (i.e., the people not found using either approach).

However, one can estimate (d) by modelling the behavior of the contingency table. Using the marginal counts—($a + b$) and ($a + c$)—the log linear models can be created to estimate (d), the number of cases missed. In addition, the standard error of (d) can be estimated. Combining this information with that in the table, N (the size of the closed population) can estimated with a standard error around this estimate.

The accuracy of the capture-recapture method depends directly on the completeness of the individual lists upon which it is based. If both lists are very complete, the cell labeled a will be large and the cells labeled b and c will be small. This means that both lists were fairly complete, with a small resultant d. If the two lists are not very complete, however, cell a will be small relative to cells b and c. The net result is that cell d will be large, and will have a large standard error, indicating lack of precision in the estimates.

A capture-recapture census works best when each list is as complete as possible, and when multiple lists are available to estimate the missing cell. Our design incorporates provisions for both these activities. By contacting 10 provider-types, using an incentive for prompt responses, and aggressively following up every letter sent out, we maximize the chances that every target case in Massachusetts will be reported. For the capture-recapture methodology, we are able to compare all children on the educational and medical lists. For further verification of overlap, we may also compare children within the medically identified lists and within the educationally identified lists.

PRE-AWARD EVALUATION

Originality and Importance

The need for an adequate data base for children dependent on medical technology has been recognized at national and State levels. As the number of children requiring this care increases, and as delivery of care moves from the hospital to the community, there is a need for better data in order to revise care services and health policy. The proposed 3-year study would provide such a data base for one northeastern State. The effort would follow methods used in Project School Care in 1987 to obtain a similar data base. The principal investigator makes a strong argument that the proposal responds to a need identified by the Technology Dependent Children Task Force of the U.S. Department of Health and Human Services and the Department of Education.

The investigator suggests (and documents) that other States might join in data collection, which would provide initial efforts toward a national data base. However, there might be a more efficient means of collecting these data, such as using the 1990 national census process, or using collaborative funding by several Federal agencies to obtain national data, rather than State-by-State efforts.

Regional and National Significance

There is a need for these data nationally, while the proposed study is statewide only. The issue, however, is important to health care providers, educators, and health policymakers, and has potential national significance. At this point, the numbers of children affected are not large (2,000–100,000 nationally), but those numbers are expected to increase and the impact of a technology-dependent child on family and community resources is sufficient to warrant increased attention to this area.

Scientific and Technical Merit

The problem is clearly stated and the investigator makes a good argument for how the data base developed in this study would assist providers in improving services. The review of the literature is organized and current. It addresses changes in health care, including technological advances, disease-specific changes in technological treatment, a new disease entity that leads to chronic care needs (AIDS), and generic issues for technology-dependent children. The investigator cites research she conducted in 1987 to provide a statewide data base, and identifies strengths and limitations in the previous design, as well as plans to address limitations.

Nine hypotheses are stated relating to the number of children dependent on medical technology in Massachusetts. They are testable and relate to the problem under study, although the literature review does not clearly relate to each hypothesis. Definitions are provided and some are clear. Standardized accepted definitions are used when possible and sources of definitions are documented. However, the way in which multiple anomalies will be handled is unclear. There is a real possibility of both multiple etiologies and multiple technologies being used for varying lengths of time. There is no discussion of this potential problem or of how it will be handled.

The measurement plan proposed closely follows that used in Project School Care. Much of it seems reasonable and was used previously with success. The measure of cognitive ability appears to be a rough estimate by educators. The use of several sources to identify children for the census is a strength. The investigator proposes using 1990 census data to estimate prevalence of medical dependency, but admits that data will not be available by the end of the study (1992).

The capture/recapture design is an appropriate one. Response rates and followup periods were problematic in a prior study, so procedures to help overcome those problems have been planned. Using a design that was previously successful, as well as providers familiar with the investigator, add to the strength of the study. However, the proposal does not indicate how the 1990 Federal census data are to be used to derive estimates of the total number of technology-dependent children in Massachusetts. It is also not clear how this estimating operation relates to the capture-recapture technique for estimating the total number of children in Massachusetts, ages 3 months to 18 years, who use some form of medical technology.

Criteria for inclusion in the census are provided, along with a detailed description of the census plan and followup contacts. Ten provider groups will contribute to two census lists. The rationale behind the selection of the age range to be studied is clearly described. Incentives to participate are mentioned, but not explained.

The data analyses are carefully outlined, including plans to ensure accuracy of data input, treatment of data that are missing in 1990 but were present in 1987, and management of duplicate data. Data will be examined by disease etiology and organ system involved. The data base will be developed, using cross-sectional and longitudinal data. The longitudinal base will allow focus on the individual, changes over time in the aggregate, and changes in the composition of the population over time. Adequate time is planned to manage this potentially large data set (in excess of 1,000 subjects). However, it is not clear whether three different 1-month periods will actually be used (given that a 1-month period of prevalence is being used, but that 3 months are allocated to identify informant sources).

A PARENT-FOCUSED INTERVENTION TO REDUCE PAIN DURING PROCEDURES

GRANTEE Trustees of Health and Hospitals of the City of Boston

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PROJECT NUMBER MCJ-250602

PROJECT PERIOD 10/01/90–09/30/93

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	149,307	123,105	123,106	n/a	n/a
Requested	149,307	152,403	165,650	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

Ill children undergo painful, invasive procedures including venipuncture, intravenous cannulation, suprapubic aspiration, and lumbar puncture during visits to the physician. Frequently, children must undergo these painful procedures without the comforting presence of their parents, who are usually asked to leave. Thus, children are stressed by both the painful experience and the lack of a comforting parent. This study investigates whether a simple parent-focused intervention can reduce the children's experience of pain during common, invasive pediatric procedures.

Research Questions or Hypotheses

No information is available about the effect that comforting parents have on either their child or a physician if they are present during an invasive procedure performed in a pediatric emergency room. The specific hypotheses of this study are that: (1) A simple parent-focused intervention will reduce the pain experienced by children during invasive pediatric procedures; (2) the intervention will be more effective than either having a parent present but with no instructions given, or not having a parent present; (3) procedures will be more successful when a parent is present and using a focused intervention; (4) the parent will demonstrate less anxiety if present during the procedure; and (5) physicians will become accustomed to the presence of the parents.

Study Design and Methods

This study is a randomized clinical trial, with three groups: (1) Parent present, instructions given for parent-focused intervention; (2) parent present, no instructions given; and (3) parent not present. Equal numbers of parents and physicians are recruited into the three groups. The three-group design was chosen to allow the following three comparisons: (1) Parental presence with instructions compared to parental presence without instructions; (2) parental presence compared to no parental presence; and (3) parental presence with instructions compared to no parental presence.

Subjects are randomized, using a technique developed by Zellin, referred to as prerandomization. Traditionally, informed consent is obtained prior to randomization. With this technique, subjects are randomized prior to obtaining informed consent.

The physician determines whether a child needs venipuncture or intravenous cannulation. The research assistant is then notified, consent is obtained, and the questionnaire is completed, including the State Trait Anxiety Inventory. The Infant Behavior Rating Scale is completed prior to the procedure. During the first 30 seconds following the initial procedure, the child's cry is recorded; during 30–60 seconds postprocedure, adopted facial coding is completed; and during 60–90 seconds postprocedure, the Infant Behavior Rating Scale is completed. Following the procedure, the parents complete a project-specific questionnaire.

Population Description and Sampling Plan

Parents and children are eligible to participate in the study if: (1) The parents consent, (2) they have not participated previously, (3) the child is less than 3 years of age, (4) the child has no history of chronic illness, and (5) the parents speak English or Spanish.

The sample size calculations are based upon four of the outcome measures and assumed an alpha of 0.05 and a beta of 0.8. Using the fundamental frequency of the cry as an outcome, a sample size of 393 is needed.

Analysis Plan

Measured independent variables are: (1) Parent present, instructions given; (2) parent present, no instructions given; and (3) parent not present. Critical outcomes of interest include: (1) Pain of the infant, measured by the Infant Behavior Rating Scale, analysis of cry, cortisol level, and global scores of pain completed by the physician involved, the research assistant, and the parent; (2) success of the procedure, measured by length of time of the procedure and number of attempts needed to obtain blood or start the intravenous cannula; (3) anxiety of the physician and parent, recorded by the State Trait Anxiety Inventory; and (4) satisfaction of care, measured by a project-specific questionnaire. Prior to analysis, the randomization process is assessed. If successful, chi-square will be used to compare categorical variables, and *t* tests will be used to compare continuous variables.

PRE-AWARD EVALUATION

Originality and Importance

The proposed investigation is both original and very important. Utilizing parents as a potential aid in analgesia is a simple and straightforward concept and one which has great face validity. But, as the principal investigator details, there are no direct data that bear on the question of whether parents can serve such a role for their young children. This is an important topic, because it is an issue faced daily in various medical clinics and hospitals when children are brought for care requiring some invasive and potentially painful procedure. Certainly, a more humane approach to providing care to young children would involve parental presence to serve as a calming influence, but parents are often excluded during medical procedures. Data from the proposed investigation will be important in developing suggestions for more humane and effective approaches to treating children. Accruing objective empirical evidence that the presence of a parent will actually reduce pain and increase success will no doubt be necessary to bring about change in the way such procedures are handled, and the proposed research could serve such a function.

Regional and National Significance

The proposed research is of national significance in that the problem addressed can be seen daily and the proposed intervention could be applied routinely in hospitals and clinics around the country. Developing more appropriate health care services for children who experience painful, invasive medical procedures is a national concern.

Scientific and Technical Merit

This is a well-developed and carefully conceived project that addresses a simple yet fundamental question in the provision of health care to children. The principal investigator presents a sophisticated and concise discussion of the issues involved in reducing the pain of invasive medical procedures for children, and the use of parental presence as a critical factor in providing a less painful experience for children. The principal investigator deserves much credit for an excellent job of integrating behavioral, developmental, and medical research literatures that bear on the issue at hand. The case made by the principal investigator for the research is convincing; this is potentially important work.

There are notable strengths to the proposed research. First, the basic design is strong. The randomized clinical trial approach to addressing the question is solid, and the use of three groups, two of which serve as controls for the intervention group, allows for the important comparisons to test the effectiveness of the intervention. Furthermore, the large sample involved (more than 1,000 cases) will allow for great confidence in the results and for their generalization to similar populations. In addition, a particularly appealing aspect of the study involves the multiple measurement approach to the major dependent variables of interest. This is true for the indices of child pain, which actually involve four measures of pain from three distinct levels: Behavioral/emotional, endocrinological, and neurological (cry). Similar attributes can be found for the measures of procedure success and parent or physician anxiety. This is a laudable strategy and likely to produce findings of some significance.

While the strengths of the study are significant, there are a number of issues involved with the proposed investigation that require further clarity or thought. First, the intervention simply involves telling the parents to talk to their child throughout the procedures and touch the child's face or hold the child's hand. Parents are told that it is acceptable if the child cries, and are asked to avoid telling the child that the procedure will not hurt. There is little evidence, however, that such an intervention is likely to produce a state of relaxation in the child above and beyond whatever the parent's presence can bring. To some degree, this is an empirical question that can be addressed in the data analyses, but the purpose of conducting the study is to determine the success of this intervention. Parents in the present-only group are not given the instructions, but it is hard to imagine that many parents will not engage in behaviors similar to the intervention as part of their natural parenting (intervention or not). How will this be controlled? Will the research assistant collecting the data also code the degree to which nonintervention parents speak to and touch their children? These are important empirical questions, but the strength of the research overall may well rest more on the concept of parent presence than intervention.

The hypotheses are generally well formulated, but the last one seems to have little justification or empirical support. Why is it hypothesized that children will have shorter hospital stays if their parents are present during invasive procedures in the emergency room and are provided a simple intervention strategy to reduce the experience of pain? The principal investigator notes that this hypothesis reflects his experience, but this is not sufficient to make such a conceptual jump. What mechanism might underlay this relationship?

In relation to the measures, there is some question as to the viability of using Izard's coding system of facial expression of emotion during the 30-second period following venipuncture. This is an incredibly complicated coding regime, which, historically, has required intense attention to high quality videotaped sequences which can be replayed slowly or even frame by frame. How such a complex coding task could be accomplished in this brief period is not clear, nor is the suggestion that it can be done convincingly without some pilot data. Furthermore, how will reliability of the ratings be obtained, given that only one research assistant will be involved in data collection? Overall, quite a lot of data collection and coding are to be accomplished in the brief 90-second episode following the venipuncture. Pilot data suggested this is a feasible strategy that would be helpful.

The heart rate data, no doubt, will prove interesting, but the presentation of the method of data collection was confusing. It is not clear exactly when and for how long parents and physicians will be hooked to the monitor. Will this be before and after the procedure, or also during the procedure? A little more clarity would be helpful. Finally, the power analyses presented are confusing. It makes little sense to treat each question of the study as a separate entity with its own sample size needs, and then use some method of combining the sample needs across the questions. A sample of 1,020 is more than sufficient to adequately address the questions at hand, and is likely more than will be needed.

The role and behavior of the nurse who holds the child during the procedure must influence the child's or parent's behavior. This is not mentioned in the protocol. Some standardization of the nurse's role must be designed to preclude functioning as surrogate parent in their absence.

No informed consent form is included in the application. Obviously, it is not a full informed consent procedure. Therefore, there must be three different forms; parents will not know of the complete study since they will be prerandomized.

The budget seems appropriate to the scope of the work. It could be argued, however, that half as many subjects could be seen with little risk to power considerations, given the questions to be addressed and the analyses to be run. This could result in a less expensive project that may have just the same impact.

PREDICTING TEENAGE PREGNANCY

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PROJECT NUMBER	MCJ-260585				
PROJECT PERIOD	10/01/89–4/1/93				
COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	187,345	168,484	185,393	50,274	n/a
Requested	185,671	188,620	185,393	50,274	n/a
* Indirect included					

SUMMARY

Statement of the Problem

Adolescent mothers are at high risk for maternal morbidity and mortality. In addition, adolescent pregnancy is highly related to risk of low birthweight and infant mortality. Children of adolescents are also more likely to be at risk for socioemotional problems and cognitive deficits than the children of older women.

In order to develop preventive intervention strategies for adolescent pregnancy, those adolescents who are at risk for pregnancy must be identified and the antecedent risk factors must be understood. Based on a review of the literature as well as theoretical considerations, this project takes the position that there are probably a number of different causative complexes that account for adolescent pregnancy. Rather that seeking a homogeneous profile of the adolescent who is at high risk for pregnancy, cluster analyses are used to identify various pregnancy risk profiles. The set of characteristics determining each profile should be useful in indicating potential intervention strategies that are most likely to be effective in reducing the risk for the adolescents exhibiting that profile.

This project is designed to identify sets of profiles for ninth grade girls and sets for ninth grade boys. These adolescents are then followed through the end of the 11th grade, and the profiles found in the ninth grade are related to pregnancy outcomes by the end of the 11th grade. The study examines gender, racial, and ethnic differences in profiles.

Research Questions or Hypotheses

This study tests the hypothesis that results of the cluster analysis will yield several distinctly different profiles of risk indicators for boys and for girls. Profiles consist of subgroups of factors from the 17 possible predictor variables examined. Gender differences in profiles are predicted (e.g., low self-esteem may be more important as a risk factor for girls, and academic achievement as a risk factor for boys). Six different profiles are tested (two for boys, four for girls), using different combinations of the predictor variables. For example, among girls of lower socioeconomic status who carry pregnancy to term, we expect to find a profile associated with coming from a single parent household, having an external locus of control, and exhibiting poor school performance.

Study Design and Methods

This study uses a longitudinal, prospective design to predict adolescent pregnancy and childbirth. Approximately 3,800 male and female adolescents from 7 school districts located in 3 counties in the Detroit metropolitan area are assessed in the ninth grade and again in the 10th grade. Social, psychological, and background factors are measured using self-report questionnaires, teacher ratings, and school records. The respondents are followed over a 2-year period, and pregnancy-related dropouts are verified at 2-month followup intervals. After 32 months, when the respondents are at the end of 11th grade, self-reports of pregnancy experiences, including abortion and miscarriage, are assessed. Self-reports are also obtained from school dropouts.

The focus of the data analysis is to identify a small number of pregnancy risk profiles, or patterns, among the antecedent factors that predict subsequent pregnancy and childbearing for different types of adolescents. Patterns among the predictors are assessed separately for male and female adolescents. The pregnancy risk profiles are used as a basis for developing specific preventive intervention strategies for subgroups of adolescents.

Demographic and background factors measured include race, family structure, socioeconomic status, and age at menarche. Social, school, and family variables include social supervision/control, domestic responsibilities, family stress, school stress, extracurricular activities, stressful life change events, satisfaction with social support network, peer relations/popularity, and antisocial influences. Psychological variables include planfulness or future orientation, self-esteem, assertive communication skills, and locus of control. Information on verbal and math achievement test scores, discrepancy between normal and attained grade, grade point average from eighth grade, absence records, and disciplinary records are obtained from school records.

At the end of the project period, when currently enrolled participants are at the end of the 11th grade, a short self-report measure of life events is administered during the homeroom classes of the original study participants. Questions about pregnancy experiences are embedded in this list. Girls are asked if they became pregnant; boys are asked if they caused someone to become pregnant.

Population Description and Sampling Plan

The sample for collection of predictive measures is restricted to ninth grade students, most of whom are between the ages of 13 and 15. The ninth grade is a good time to reach at-risk adolescents, before many of them have become sexually active.

The sample is selected to be diverse in sociodemographic characteristics. The use of schools from communities with heterogeneous populations, in a metropolitan area with a relatively high rate of adolescent pregnancies, should facilitate detection of various pregnancy risk profiles. Seven school districts were selected from three counties in the Detroit metropolitan area. The combined number of ninth graders in these 7 districts was 3,745 in the fall of 1987.

Preliminary information from the school districts indicates a 95 percent consent rate. We estimate a 15 percent loss due to lack of consent, transfer from the school district, and failure to locate. We estimate a total of 297 pregnant girls (155 white, 142 black), and 240 boys causing a pregnancy (129 white, 111 black). These numbers are more than adequate for the cluster analyses described in the analysis plan.

Analysis Plan

The main purpose of the analysis is to examine the extent to which profiles of variables, determined in ninth grade, predict the adolescent pregnancy experiences of both girls and boys within the next 2 years. The study tests the hypothesis that there are several different patterns of traits that are likely to be related to adolescent pregnancy experiences, rather than one reason for all adolescents.

Internal consistency reliabilities (coefficient alphas or Kuder-Richardsons) are computed for all the measures. Initial data analysis includes varimax factor analytic techniques in order to combine and collapse the 17 measures into factor scores appropriate for cluster analysis. The following factors are expected: (1) A general school stress factor will be found on which the academic adjustment measures from the school records and the self-reported school stress index will load highly; (2) a popularity factor will be found in which the teacher ratings of popularity and attractiveness, the sociometric measure, and the self-reported index of peer relations will load highly; (3) measures of occupational and educational goals and the two scores from the Future Events Test will load on a general planfulness factor; and (4) a family stress factor is expected on which the measures of paternal and maternal relationship quality will load. Scores for the identified factors (constructs) will be computed by using average *z* scores.

Major data analysis techniques employ cluster and linear discriminant function analyses (LDFA). The determination of profiles consists of two sets of analyses. The first set of analyses consists of a cluster analysis to determine empirically the dominant profiles of the relevant variables, as these emerge in the adolescent sample. These profiles are compared with the adolescent pregnancy experiences of the persons constituting each profile, to determine which profiles are most likely to be associated with pregnancy experiences.

The second set of analyses involves a linear discriminant function analysis. This LDFA was designed to evaluate the efficacy of the profiles as predictors of pregnancy experiences. Separate profiles will be determined for girls and for boys.

We employ Ward's method, which appears to provide the tightest fit of the various methods proposed in the literature. A cross-validation design is used to determine profiles, and to evaluate their relationship to adolescent pregnancy.

PRE-AWARD EVALUATION

Originality and Importance

This project could contribute substantially to an understanding of the antecedents of adolescent pregnancy. The strengths of this project are its prospective, longitudinal design, which will allow causal variables to be identified; its focus on male as well as female adolescents; and its attempt to develop profiles of different risk groups. The latter is a clever and original approach which, if successful, has important implications for education and intervention.

Regional and National Significance

Adolescent pregnancies are a burden for society as a whole and have negative consequences for the adolescent mother and her infant. Therefore, the information to be obtained from this project is of national relevance. The analysis of risk profiles can be used to develop interventions that target subgroups of adolescents at risk for early pregnancy and childbearing. Moreover, the sample to be used is large, comes from several communities in a metropolitan area with a relatively high rate of adolescent pregnancy, and is demographically diverse. These factors should help ensure the generalizability of the findings.

Scientific and Technical Merit

This is a resubmission of a proposal that was previously approved but not funded. It is a large-scale, ambitious project on the antecedents of adolescent pregnancy and addresses several lapses in the literature: The need for careful, prospective studies of adolescent pregnancy, the need to include males as well as females in the study population, and the attempt to differentiate risk groups.

The literature review is clear and thorough. The variables to be studied are closely derived from this review, as are the hypothesized risk profiles. The investigators have nicely balanced the need for broad, intensive assessment with the need to assemble an assessment package that is easily and quickly administered.

The constructs are clearly specified. Most measures are reliable and have been found in other research to differentiate adolescents continuing their pregnancies from other control groups. Few of these variables have been examined in a prospective design, so previous research has not been able to clarify whether they predict or are merely correlated with adolescent pregnancy and childbearing. Therefore, this untangling of causal relationships will be an important contribution of this project. Selecting variables that have already been carefully studied firmly grounds the research and also suggests that the novel contribution of this project is its sophisticated data analysis strategy, applied in a prospective design, rather than in identifying new variables which might predict adolescent pregnancy.

There have been few prospective studies of adolescent pregnancy, partly because of the costs entailed in doing such research. By recruiting subjects through school districts and limiting the assessment to a manageable size, the investigators present a relatively cost-effective way of conducting this much-needed research. Pilot testing indicates that good cooperation with the procedures can be obtained. The investigators' rationale for recruiting ninth grade subjects is convincing, because there appear to be few live births among adolescents in the ninth grade or younger in their subject pool. The investigators have developed adequate procedures for tracking such a large subject pool, which is a crucial aspect of the study. They also have carefully estimated the number of pregnancies that will occur during the study period, and the numbers appear adequate to conduct the kinds of analyses planned.

The data analyses are well specified and appropriate for the data. For instance, the investigators show sensitivity to the limitations of their approach in not being able to obtain data on sexual activity or contraception.

This revision generally attempts to deal with the criticisms of the previous proposal. In response to concerns about whether males may underreport their pregnancy experiences, the investigators cite research on adolescent drug use and delinquency that suggests that adolescents are generally honest in responding to survey literature. However, this research also indicates that adolescents are more honest when they know their responses will be checked (e.g., when self-reported drug use is supplemented with chemical analysis). In addition, as there is nothing analogous in this study to checking criminal records or conducting chemical analyses, there will be no way to check the veracity of reports. Since some males may not be aware of pregnancies they caused, there is a possibility of systematic bias. However, there is little that can be done to directly address these concerns, and despite these potential problems, the inclusion of males is a strength of this proposal.

This revision still lacks a developmental perspective, although some efforts have been made in this direction. A stronger developmental focus, including the addition of developmental variables, might strengthen the predictive power and the strong social-psychological and personality perspective of this proposal. Finally, the investigators provide clearer evidence in this revision that the study could proceed adequately if a smaller sample than estimated is enrolled in the study. Obtaining parental consent still appears to be a major obstacle to the success of this study, and no procedures to increase parental cooperation are detailed.

This project will require an estimated 3 years to complete. This time schedule seems optimistic, given that subjects will be followed for more than 2 years, but since the bulk of the data collection occurs early in the project, it may be feasible.

FEEDING METHOD AND FAT TOLERANCE IN VERY LOW BIRTHWEIGHT NEONATES

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PROJECT NUMBER	MCJ-260596
PROJECT PERIOD	10/01/90–09/30/93

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	234,696	200,871	209,931	n/a	n/a
Requested	234,696	200,871	209,931	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

The purpose of this investigation is to determine the effects of two different, widely used means of feeding very low birthweight neonates enterally (nasogastric continuous drip and intermittent bolus feeding) on physical growth, gastrointestinal tolerance, rate of progression of feedings, and macronutrient balances. The study also seeks to determine how abnormal lipid patterns observed in plasma of very low birthweight neonates who receive fat emulsion parenterally compare to lipid patterns observed in plasma of neonates of similar birthweights who are being fed enterally with a formula containing 50 percent of its fat as medium chain triglycerides.

Research Questions or Hypotheses

The study examines the following hypotheses:

Aim 1: We hypothesize that continuous nasogastric feeding permits faster rates of growth and therefore shorter duration of hospitalization. We further hypothesize that this beneficial result is due to a combination of more rapid progression of feedings (in volume and concentration of formula), better tolerance of the feedings, and more efficient digestion of macronutrients (evidenced by retention of carbohydrate, nitrogen, and fat as estimated by metabolic balance studies).

Aim 2: We hypothesize that, at certain rates of infusion of parenteral fat emulsions, plasma lipids are no higher than those observed in neonates of similar birthweight and gestational age who receive enteral feedings only with formulas containing 50 percent of their fat as medium chain triglycerides. Therefore, neonatologists should either (a) not be concerned about these relatively elevated plasma lipids in parenterally fed premature babies, or (b) they should be, but currently are not, equally concerned about plasma lipid profiles in enterally fed babies.

Study Design and Methods

All neonates who enter the study are cared for in the same environment and by the same personnel as the nonstudy babies. In order to generate data that are directly applicable to the clinical situation, only the method of nasogastric feeding and the formula used during the period of nasogastric feeding are predetermined by the protocol of the study. To minimize the risk of obscuring the results of the study because of individual bias by the various neonatologists and staff members who actually take care of the neonates, all decisions concerning feedings are made by the principal investigator or by a research nurse under the principal investigator's supervision. Such decisions include, but are not limited to, the following: (1) Start of enteral feeding; (2) progression of feedings; (3) interruption of feedings, if necessary; (4) time at which to give parenteral supplements; and (5) time at which to introduce feedings by nipple and discontinue nasogastric feeding.

Before starting hypocaloric feedings on the third postnatal day, the method of feeding is determined from a sealed envelope. Henceforth, that method of feeding is used until it is decided to introduce nipple feedings. At that time, the protocol officially ends. Data collection, however, continues until the neonate reaches a weight of 1,800 grams or is discharged to home, whichever comes first.

All neonates are fed a whey-predominant formula (Similac Special Care 80 Kcal/dl), because this formula is widely used in nurseries around the country, and because it has the potential for more complete absorption of fat than other formulas.

At the time of entry into the study, the infant's medical record is reviewed in order to determine the Severity of Respiratory Distress (SRD) score.

In order to investigate the hypothesis of Aim 2, we conduct a "ministudy" of plasma lipid levels to determine the effect of the mode of feeding and of a given rate of enteral lipid intake. This is performed as soon as possible after the neonate has reached a caloric intake of 100 Kcal/kg/day without any parenteral fluids. During 4 days, the neonates receive 125 ml/kg/day of formula. In group I, plasma samples are obtained before a feeding and again at 30, 60, and 120 minutes after feeding on day 4 of the study. In group II, plasma samples are obtained every 6 hours on day 4 of the ministudy.

Population Description and Sampling Plan

All neonates of normal growth, weighing between 750 and 1,499 grams at birth, with a gestational age of 27 weeks or more, are potential candidates for the study. Ninety babies are studied in 2 groups, each comprised of 45 subjects. In order to ensure an even distribution of birthweights in each study group, each group is subdivided into 3 subgroups of 15 subjects each, with birthweights of 750–999 g, 1,000–1,249 g, and 1,250–1,499 g, respectively. Babies in group I are fed by continuous nasogastric drip; babies in group II are fed by nasogastric bolus every 3 hours. Subjects, stratified by birthweight, are assigned randomly to one of these two groups at the time they are deemed ready to be fed enterally according to clinical criteria prevalent in our nursery. Randomization is accomplished at the start of the study by preparing sealed, opaque envelopes containing a card with group assignment derived from a table of random numbers. At the time of study, demographic and medical data are collected on each subject, including sex, postnatal age, intercurrent illnesses, and other information.

Analysis Plan

The demographic and medical data are analyzed to compare the two groups and their subgroups and to ensure that they are similar in terms of severity of illness. With the number of subjects involved, it is expected that randomization will produce comparable groups. In our previous study of parenteral fat emulsion, we found that randomization of 45 neonates into 3 groups of fat intake, using stratification similar to that used in this study, produced three groups with comparable distribution of $AaDO_2$ at the beginning of the study. However, SRD score is used as a covariate. The various indicators of respiratory function are compared for the groups and subgroups. Since the data are unlikely to be normally distributed, nonparametric tests are used.

Aim 1: For comparisons between intermittent bolus and continuous feedings, weekly changes in anthropometric measurements, mean weekly volume and caloric intakes, weekly lipid levels, and results of macronutrient balance studies are compared between group I and group II (and the relevant subgroups) by analysis of variance for repeated measures and adequate post hoc tests (Duncan's multiple range test). A *p* less than or equal to 0.05 is required to reject the null hypothesis (i.e., that there is no difference between the two methods of feeding). Attention is paid to the time needed for each group of neonates to reach feeding milestones (i.e., time to reach full enteral nutrition, switch to nipple feeding, switch to regular formula, reach 1,800 grams) and to the occurrence of necrotizing enterocolitis, necrotizing enterocolitis "scares" (abdominal distension without radiological signs of necrotizing enterocolitis), and feeding formula intolerance. Special attention is paid to differences in outcome during the period of gavage feeding of 80 Kcal/dl formula.

Aim 2: The effect of bolus enteral feedings on concentrations of plasma lipid during the 4-day ministudy (group I) is determined by comparing the mean plasma lipid concentrations at each of the four sampling times by analysis of variance for repeated measures and adequate post hoc tests (Duncan's multiple range test). A $p \leq 0.05$ is required to reject the null hypothesis (i.e., that time of sampling in relation to feeding time does not affect concentration of the various lipid fractions in plasma).

In determining the effect of method of feeding on concentrations of plasma lipids during the ministudy, results for all four measurements are averaged, since neonates in group I are fed under "steady state" conditions and concentrations of lipids in plasma are not expected to vary significantly. Preliminary data suggest that only minor fluctuations in plasma lipid concentrations occur in relation to a feeding. If this is confirmed in the present study, results of the four measurements will be averaged. The average of the measurements observed in group I is compared to the average of the measurements observed in group II by Student's *t* test of two means. If the data for group I indicate clinically significant differences with time after a feeding, the average of the measurements obtained at each sampling time is compared to the average of the measurements observed in group II by Student's *t* test of two means. Since four comparisons are performed on the same set of data, a $p \leq 0.01$ level of significance is required to reject the null hypothesis (i.e., that method of feeding does not affect concentrations of the various lipid fractions in plasma).

Plasma lipid patterns observed previously in parenterally fed neonates are compared to those observed in enterally fed neonates (no statistical analysis is possible).

PRE-AWARD EVALUATION

Originality and Importance

The first aim of the study is original and potentially very valuable. This portion of the study is clinically significant because data related to the effectiveness of the two methods are extremely scarce, and thus neonatologists arbitrarily choose a feeding method according to their biases, without availability of sound scientific data. The authors speculate that slow constant feeding (continuous nasogastric feedings) may decrease physical disturbances of the neonate and gastric distension, both of which may play a role in apnea spells. In addition, they speculate that continuous nasogastric feedings may improve utilization of nutrients at a lesser energetic cost and thereby improve weight gain and the composition of weight gain.

The second aim of the study is to discover the plasma lipid patterns of enterally fed very low birthweight babies under prevailing nursery conditions. These data from very low birthweight babies fed enterally can be used for comparison with plasma lipid patterns of babies fed parenteral fat emulsions. The data would provide a basis for the development of recommendations related to the amount of parenteral fat emulsion that can be given to various weights and/or groups of very low birthweight babies. Both of the study aims will provide data that are directly and immediately applicable to everyday nursery practices and hopefully will improve health care delivery and reduce the length of hospital stay for these infants.

Regional and National Significance

The anticipated findings have national significance since both feeding methods are used extensively throughout the Nation.

Scientific and Technical Merit

This application is a revision of one reviewed and disapproved previously. The principal investigator clearly presents the rationale for the proposed study and outcome variables and persuasively argues for the envisioned applications of the study findings. He has extensive experience in completing clinical studies in low birthweight infants and a particular interest in plasma lipids in preterm infants.

The hypotheses for both study aims are clearly stated and extensively justified, with appropriate limitations noted. The thorough, critical review of available data and the discussion of the physiologic responses that might be expected with the two feeding methods substantially strengthen the proposal. In addition, the principal investigator presents data from his well-designed and carefully completed 3-year study of the effects of three regimens of fat emulsions on the plasma lipid patterns of very low birthweight infants. These data from infants who are parenterally fed fat emulsions provide the serum lipid data for comparison with serum lipid data from infants who are fed enterally (data to be obtained in the proposed study).

The study proposes to stratify subjects by birthweight and randomize subjects to either feeding group when they are ready to be enterally fed. A Severity of Respiratory Distress score will then be used to adjust for potential differences between groups in severity of illness, a known influence upon rate of weight gain of very low birthweight infants. The study design and approach to data analyses are reasonable.

The protocol for initiating and advancing feedings is explicitly defined in this revised proposal and is based upon objective criteria for gastrointestinal tolerance and interruptions. This component of the proposal will be critical to the successful outcome of the study because it minimizes the potential for investigator bias. Furthermore, the indicators selected to evaluate the effects of the two feeding methods are much more clearly defined. For example, body fat and total body water will be estimated with TOBEC (a rating scale), and the definitions for stool consistency are given.

The sample size calculations are based upon the rate of weight gain calculated from birth to discharge, and a 13 percent rate of attrition. Necrotizing enterocolitis concern will not be a criterion for discontinuing the study, and thus, the principal investigator believes that an attrition rate of 13 percent (albeit a relatively low attrition rate for clinical studies) is realistic. The number of very low birthweight neonates from Hutzel Hospital and Children's Hospital of Michigan is large enough to study 30 neonates per year, despite commitments of similar patients for other research projects.

The methods in this revised proposal are generally acceptable, with one easily corrected exception. The feeding protocol defines the initial volume of feeding on a per kg basis (18 cc/kg). Increases in volume of feeding, however, are not based on weight, but, rather, are based on time (increase 1 ml/hr every 12 hours, for a total daily increase of 36 cc/day). Therefore, the infants will be managed differently, based on weight. The smallest babies will be advanced almost twice as fast on a per kg basis by the time they are 6 days of age. It is highly unlikely that the smallest babies will tolerate this aggressive advancement of enteral volume, regardless of the method of feeding; therefore, the study will not have the capability to distinguish more subtle differences in outcome between the two feeding methods in the smallest babies (because all will fail). Advancement of feedings in the biggest babies is much more realistic and reasonable. The study would be strengthened if the protocol would define advancement of feedings in the three weight groups on a per kg basis. In addition, the principal investigator needs to state a maximum enteral volume for the advancement.

USE OF HIGH CALCIUM INFANT FORMULA TO PREVENT PLUMBISM

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PROJECT NUMBER	MCJ-330597				
PROJECT PERIOD	10/01/90–09/30/92				
COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	237,640	142,957	n/a	n/a	n/a
Requested	238,726	219,913	n/a	n/a	n/a
* Indirect included					

SUMMARY

Statement of the Problem

In October 1991, the Centers for Disease Control and Prevention published a fourth revision statement on childhood lead poisoning, emphasizing primary prevention of this disease (a departure from earlier statements). Based on data showing adverse neurodevelopmental effects of lead in young children at increasingly lower levels of blood lead (BPb), the level of concern for blood lead in children was revised downward from 25 to 10 μg/dl. This has profound implications for the diagnosis and management of childhood lead poisoning because many more children are defined as being at risk. It is estimated that 3–4 million children in the United States have blood lead levels greater than or equal to 15 μg/dl. Moreover, evidence from Third World and Eastern European countries indicates that large numbers of children in those countries are exposed to very high levels of lead, exhibiting mean BPb levels of 20–30 μg/dl (similar to those of urban American children in the 1950s); these children have high rates of lead encephalopathy as well.

In this country, deteriorating lead paint is the major source of excessive lead exposure for children. Four million American children live in houses built before 1950. The primary prevention of childhood lead poisoning will ultimately require abatement of old houses with this form of paint. This process will take years and require billions of dollars. In the meantime, children will continue to be exposed to lead in their environments. In addition, many other countries do not have the resources needed to undertake large-scale environmental decontamination. Thus, additional primary prevention strategies are needed for high-risk groups of children who live in lead-contaminated areas. These strategies should be developed to protect children between birth and 2 years of age, the period when blood lead rises rapidly in exposed children, and when the developing central nervous system is most sensitive to the toxic effects of lead.

Research Questions or Hypotheses

Calcium has been shown to competitively inhibit absorption of lead from the gastrointestinal tract in animals and humans. Phosphate exhibits an additive effect, further impairing lead absorption when given in conjunction with calcium in animals. The hypothesis tested in this study is that supplementation of infant formula with calcium glycerophosphate will lead to significantly lower blood lead levels in exposed children at the end of the study period.

Study Design and Methods

This study is a full double-blind randomized controlled clinical trial of calcium glycerophosphate-supplemented infant formula in a group of infants at high risk for lead exposure. Infants enrolled in the control group consume powdered Enfamil with Iron (0.465g calcium per liter, 0.317g phosphorus per liter) for 9 months. Study infants consume identically labeled powdered Enfamil with Iron with added calcium glycerophosphate (1.8g calcium per liter, 1.39g phosphorus per liter) for 9 months.

The safety of this supplementation will be evaluated. Infants have never received supplementation equal to the levels of calcium and phosphorus used in this study. With respect to potential adverse reactions, we are evaluating the possibilities that (1) increased absorption of calcium will lead to increased urinary excretion of calcium or hypercalciuria in supplemented infants; and (2) infants who receive supplementation will absorb less iron than infants who do not receive supplementation.

Acceptability of the formula will also be evaluated. Inherent in the success of any infant formula is the infant's tolerance of the formula and the mother's perception of tolerance. We are monitoring supplemented infants for side effects that may lead to decreased acceptance, such as constipation, diarrhea, and vomiting.

Finally, the efficacy of the intervention will be evaluated. The primary outcome measure for this trial is the difference between blood lead at 9 months after randomization and entry into the study (Δ BPb$_9$). As an evaluation of efficacy, we will compare Δ BPb$_9$ for control versus supplemented infants.

Infants ages 4–7 months are randomized after a 1-month run-in period to assess eligibility, short-term tolerance of calcium supplemented formula, and compliance with return visits. Randomized infants have blood drawn for BPb, serum calcium, phosphorus, hematocrit, and markers for iron status at baseline, and again at 5 and 9 months following randomization. Concurrent with blood tests, a 3-day dietary analysis for calcium and phosphorus is performed. Infants return monthly for measurement of height and weight, formula distribution, analysis of urine for blood and calcium excretion, and reassessment of infant formula tolerance. The calcium content of infant formula is decreased for those infants who develop possible adverse effects of added dietary calcium (hypercalciuria, hematuria).

The study gathers data on covariates of blood lead, including lead content of house dust and drinking water, timing of meals, and iron status. Environmental dust samples are collected by placing a doormat inside the main entrance of each household. After 1 month, dust samples vacuumed from these mats are analyzed for dust lead content. Drinking water samples are collected from the water source used by the family in preparing infant formula.

Population Description and Sampling Plan

Infants recruited for this study must live in Lawrence, Massachusetts. Lawrence is a manufacturing city of 60,000, located on the Merrimack River approximately 30 miles north of Boston. Most of the housing consists of wood frame two- and three-family houses built in the early 1900s, when Lawrence was a manufacturing center. The quality of this housing stock has deteriorated in the last 40 years as owners have moved out of the Lawrence area. The last wave of Irish immigrants who worked in the Lawrence textile mills has been replaced by an Hispanic immigrant population from Puerto Rico and the Dominican Republic. Lawrence now has one of the highest poverty rates of any city in the State. The majority of infants in the study are living within a geographic area at high risk for environmental lead contamination. Consequently, Lawrence has one of the highest rates of lead poisoning in Massachusetts: In 1990, 2.5 percent of the children ages 1–2 years who were screened had blood lead greater than or equal to 25 mg/dl. No population-based data are available on mean blood lead.

Potential participants are assessed by a two-tier system during the run-in period. The primary exclusion criteria eliminate subjects on the basis of information that can be obtained by interview. All primary caretakers whose infants satisfy these criteria are asked to participate. Those who agree are then assessed by a set of secondary criteria which require (1) a blood lead measurement, (2) a test for hematuria and hypercalciuria at baseline and after a 2-week trial of calcium-supplemented formula, and (3) permission from the infant's primary care physician.

The primary exclusion criteria include the following: (1) The infant's primary address is not within the defined geographic risk area; (2) the infant is currently receiving multivitamin supplements and the primary caretaker wants to continue supplementation; (3) there is a medical history of kidney stones in a sibling, parent, grandparent, or parental sibling; (4) the infant is not currently receiving cow's milk-based formula (Enfamil with iron); (5) the infant's gestational age is less than 34 weeks; (6) the infant has rickets, parathyroid dysfunction, or recent fracture; (7) the infant is taking chronic medications; (8) the infant's height or weight is less than or equal to the 5th percentile for age; and (9) the infant is not insured for health coverage.

The secondary exclusion criteria include the following: (1) The parent does not agree to participate or give informed consent; (2) the primary care physician refuses to participate; (3) the infant's blood lead is greater than or equal to 25 µg/dl; (4) the infant has hematuria (greater than or equal to 5 RBC/high power field) that is not related to a urinary tract infection; and (5) the infant has hypercalciuria at baseline or develops it in response to a 2-week trial of calcium-supplemented infant formula.

Analysis Plan

The primary metric in this study is a comparison of the $\Delta\ \mathrm{BPb}_9$ of members of the treatment groups. In addition, since the purpose of this intervention is to prevent the toxic effects of lead exposure, the proportion of children whose blood lead levels exceed a specific threshold may be examined.

Consistent entry criteria apply to these infants; therefore, many of the variables for which we are collecting data will be homogeneous throughout the study population. The individual infant is the unit of randomization, observation, and analysis, and inference is drawn on the effects of the intervention.

Many of the variables are expressed in terms of a within-treatment group proportion, a change in proportion, a difference in log mean between groups, or a change in log mean between entry to the study and discharge. We explore the hypothesis that the blood lead levels change differently over time by treatment group. This hypothesis is tested by the use of repeated measures of analysis of variance (ANOVA), using the $\Delta\ \mathrm{BPb}_9$ as the dependent variable to be analyzed in order to assess the treatment effect.

Since this is a randomized trial, patient characteristics should be similar in each of the treatment cells. Nevertheless, data on important covariates is collected so that we can verify that randomization yielded equivalent treatment groups, and so that multivariate analysis may be used to adjust for any imbalances noted between the control and experimental groups. Logistic regression analyses are used to examine the relationship between exposure to the intervention program and outcome while controlling for important covariates. Stratified analysis by subject characteristics may break down because of smaller numbers in the analysis cells. In this case, the use of multivariate modeling may be advantageous. In all multivariate analyses, regression diagnostics are performed to aid in selecting a final model.

PRE-AWARD EVALUATION

Originality and Importance

The objective of this study is important to children and their families residing in New England. The use of a clinical trial of calcium-supplemented formula to reduce absorption of environmental lead in infants is unique. Most prior studies have used laboratory animals or adults, or have been epidemiological studies. The longitudinal experimental design should help to overcome the methodological limitations of prior cross-sectional research.

Regional and National Significance

While this trial is being conducted regionally, its potential impact is great. New England has a high incidence of lead poisoning, so the regional testing, itself, is important. If the trial shows that supplemental calcium improves blood lead levels without concomitant renal problems, then the 4 million children at risk across the country could potentially benefit from this new approach. Given the serious learning problems experienced by children with increased blood lead levels, this benefit is significant.

Scientific and Technical Merit

This is a well-written proposal, with the various parts of the research process clearly explained. The complexities of trying to conduct a study with the principal investigator in northern New Hampshire and the subjects in the greater Boston area were minimized, although the budget does reflect some of these complexities.

The problem is clearly stated, researchable, and has potential significance to alter pediatric care. The investigator cites animal studies on lead absorption related to calcium as far back as 1940, and traces the few human studies that have been conducted. He makes a solid case for applying primarily laboratory-based findings to infants. The investigator has indicated the direction of future studies after he has tested the safety and efficacy of this primary prevention strategy.

The research has one major hypothesis: Calcium phosphate supplementation of infant formula will substantially decrease absorption of lead in infants. Several specific goals are also stated, including determining the safety of calcium-phosphate supplementation, the level of calcium required to prevent lead retention, and the relation of blood lead and growth. The major variables are the amount of supplemental calcium-phosphorus, blood lead levels, measures of several covariates (race, socioeconomic status, housing status, iron intake), and markers of hypercalciuria.

The two-part hypothesis is testable and is clearly related to the research problem and the literature review. The study has a secondary goal of obtaining information on the association between blood lead levels, growth, and the iron status of children. It is not clear how the growth variable(s) will be defined. No table of variables, operationalization of variables, or levels of measurement are presented, although references to urine and blood measures are found throughout the text. The level of measurement for the blood tests can be assumed. The investigator did not address measurement of growth velocity, part of his secondary goal.

This is an appropriate, well-controlled design. A 9-month longitudinal randomized clinical trial will be conducted with families, nutritionists, and laboratory personnel blinded to treatment or control group membership. A preliminary short-term trial for compliance will be conducted, followed by the treatment, with noncompliant families excluded. Initially, the treatment group will be twice the size of the control group, but after 4 months, the treatment group will be reassigned by random selection into two equal groups of differing concentrations of calcium supplementation. The method of randomization is described. Exclusion criteria are described and will be applied in two steps. These decision points are diagrammed for additional clarity. The investigator plans weekly onsite monitoring of the study to control for treatment bias. In addition to randomization, demographic variables will be obtained so they can be treated as covariates in regression analyses, although the investigator anticipates homogeneity in the sample. Attrition is not addressed, although the small cell size for analysis is discussed.

One weakness of the design is that the 1.8 g/l group begins treatment at a different age (9 months) than the 1.2 g/l group (5 months). Of course, the 1.8 g/l group has already had dietary supplementation. Thus, this group is actually a 1.2–1.8 g/l group. This inelegance is necessitated by the desire to protect infants from hypercalciuria, and appears to be unavoidable. Future large-scale studies, hinted at by the principal investigator, could correct this problem.

A second weakness of the design concerns the link between the level of lead expected in these infants and the level which is currently the cut-off for referral. Only about 3 percent of the infants in these groups would be expected to have blood levels above 25 μg/dl. It is unclear whether prevention of an expected rise in blood lead levels in a subclinical population might generalize to infants who would eventually achieve clinical levels. This concern is outweighed at this point by the importance of establishing some relation between dietary calcium and lead levels and by the need to document any hazards associated with dietary supplementation.

Another concern is whether mothers in the control group will be adding a placebo substance to the formula. If so, what will the placebo be?

Patient compliance with the protocol will be measured by monthly counts of residual packets and by urinalysis for riboflavin, which will be added to each calcium packet. It is unclear where and how the residual packets will be counted. Is this done by mothers' reports?

Infants who have blood levels over 25 μg/dl will be referred to lead clinics (approximately three such infants are anticipated). If iron deficiency is detected, supplementation will be given. Finally, subjects who are noncompliant or who switch to lower calcium levels because of hypercalciuria will be included in their original group. This is a conservative procedure.

Two previous studies have shown that blood levels rise rapidly between 6 and 24 months. Therefore, the study will begin supplementation at 5–7 months. Would earlier supplementation be theoretically desirable? Is there a practical limitation precluding enrollment at an earlier age?

The major data analytic tools are repeated measures analysis of variance (ANOVA) and logistic regression. These seem appropriate to the task. Groups will also be assessed for differences on the covariates; if differences exist (despite randomization), they will be accounted for, using regression techniques. Subgroup analyses are hinted at (e.g., males versus females), but the small number of subjects is a recognized limitation here. The estimates of power suggest that the study's power will be sufficient to detect a 20 percent reduction in blood lead levels, which is believed to be a clinically meaningful reduction.

The study will be conducted at a host site for the Special Supplemental Food Program for Women, Infants and Children (WIC). This decision seems prudent, since the WIC site has a suitable subject population and staff to assist in the research. A letter of support accompanies the proposal.

Because the appendices (to be submitted with the proposal) were omitted, parts of the budget cannot be verified, such as laboratory equipment for blood samples. Although this is a small example, it does suggest that considerably more funds were requested than would be needed to carry out the project. The budget generally is not well justified.

Documentation of the risks and benefits to subjects is clear and adequate, and the Institutional Review Board has already approved the informed consent letter. Efforts will be made to ensure a satisfactory translation of the form into Spanish.

PREDICTING PRESCHOOL FUNCTION FROM CONTINGENCY INTERVENTION

GRANTEE University of Medicine and Dentistry of New Jersey
Robert Wood Johnson Medical School

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PROJECT NUMBER MCJ-340605

PROJECT PERIOD 7/1/91–6/30/93

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	105,065	94,498	n/a	n/a	n/a
Requested	106,362	111,174	n/a	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

Most early intervention programs for disabled infants are concerned with the acquisition of skills related to developmental milestones. This study evaluates the long-term impact of a successful intervention which is process oriented rather than skill orientated. The intensive 3-month, home-based intervention was designed to motivate the very young disabled infant to become more active in approaching the physical world. The program provided immediate, concrete, and enjoyable incentives for simple limb movements. The goal of the intervention was attained (i.e., the fostering of expectancies of environmental control and increasing motivation to explore the physical environment), and improved outcomes in experimental versus control subjects were observed.

The goal of the present followup study is to determine whether initial gains have been maintained and whether preschool status, in particular functional domains, are related to the intervention variables. The study focuses on disability rather than ethnic or racial issues. Comparisons between Down syndrome and cerebral palsy are the focus of the analysis. Gender issues are explored as a matter of course in the analysis of the data.

Research Questions or Hypotheses

The major hypothesis is that an intervention designed to promote active control of the physical environment (contingency intervention) is related to outcome measures in developmentally delayed preschoolers at 5 years of age. Participation in the program is expected to be directly associated with better functioning in the preschool period. We further hypothesize that the amount of time actually spent engaged in the contingency intervention will predict the functional status of the preschooler on a number of outcome measures.

Study Design and Methods

This is a longitudinal study. Infants are seen initially before their first birthday and receive a comprehensive developmental assessment. Background and early status variables, including demographic information, parent stress, child health, and disability status, are also gathered at this time. Preintervention measures of child developmental status include the Bayley Scales of Infant Development, the Uzgiris-Hunt Scales of Infant Development, Mother-Infant Intervention, and measures of attention.

After initial assessment, infants receive the contingency intervention at home for 3 months. Contingency play activities are administered by the mother and are computer monitored. Weekly staff support is provided for the mother. Intervention measures include the amount of time the child spends in contingency intervention as logged on the computer, and measures of child performance. Pretest measures are repeated for a postintervention assessment approximately 4–5 months after the original preintervention assessment.

All children are seen again at 4½ to 5½ years of age. By this age, they have experienced 1–2 years of preschool for the handicapped in addition to their early intervention experience, but have not yet entered kindergarten. The battery of outcome measures collected at this point include the Bayley Scales of Infant Development or the Stanford-Binet Intelligence Scale, as appropriate, the Sequenced Inventory of Communication Development, the Vineland Adaptive Behavior Scale, examiner ratings of child test behavior, and measures of play scored from videotape.

Population Description and Sampling Plan

The sample consists of 124 infants who had physical and cognitive delays at 12 months of age. They fall largely into two major diagnostic groups: Infants with Down syndrome, and infants with cerebral palsy. Infants with Down syndrome comprise about 55 percent of the sample. These subjects have been recruited from the population attending either infant intervention programs within a 30 mile radius of our university, or the neonatal intensive care unit followup clinic at the university. Both urban and suburban centers have been included. Parents volunteer for the study and receive no compensation for participation. Gender is balanced in the study. All minority groups are represented, although their representation is low (5 percent). It should be noted, however, that no special efforts have been made to recruit minorities and that compensation for travel or participation has not been built into the study. These factors may have affected minority participation.

Analysis Plan

The analysis focuses on two major questions. First, is any contingency intervention better than none? To answer this question, we compare the sample of 124 infants who received the experimental intervention with an extant normative longitudinal sample of disabled infants who received only standard services. These data are subjected to path analysis, using least-squares regression. Followup status is the major dependent measure, and contingency intervention experience (yes/no) is the major variable of interest. Health, demographic status, parental stress, and pretest status are also factors in the model. The analysis allows us to determine whether the addition of the experimental intervention contributed more to followup status than the other variables in the model.

Second, do children who received more contingency intervention experience do better in preschool than those who experienced less intervention? To answer this question, only data from those infants who received intervention and followup are considered. The measure of intervention is the amount of time (in minutes) logged in the contingency intervention program. Path analysis determines whether the amount of intervention accounts for a greater proportion of variance in the outcome variables than the other variables (such as pretest status or health status) in the model.

PRE-AWARD EVALUATION

Originality and Importance

This study will test the long-term effects of a unique, very well conceptualized early intervention program. This program, rather than concentrating on the acquisition of specific skills, builds on a large body of literature on the significance of learning experiences for infants and the interrelationship between early cognitive and affective development.

The program is not only well conceptualized, described, and operationalized, but the investigators present preliminary data to show short-term effects in four behavioral areas: Increased attention, better state regulation (more alert and less fussy), gains in overall developmental process, and evidence for generalization of experience. The proposed investigation will explore the long-term effects of this innovative and unique early intervention approach for handicapped infants.

Regional and National Significance

The proposed study will be conducted on children with Down syndrome and children with cerebral palsy. The study findings would be most applicable to these populations nationwide, although they might be generalizable to other handicapped populations. Thus, the demonstration of positive effects from this early intervention program can have implications for a large number of infants and their families.

Scientific and Technical Merit

The problem is clearly stated, with two testable research questions posed. The first uses extant data for between-group comparisons. The second uses extant data as well as some data to be collected for within-group comparisons.

The literature review is excellent. It presents a comprehensive theoretical framework, as well as empirical evidence to support the basic principles of the intervention. The intervention builds on an extensive literature on infant cognition, affective development, and learning. The proposal also provides preliminary data to support the positive effects of the intervention.

This proposal is well conceptualized and provides clear, explicit definitions for most variables, at both the conceptual and empirical level. Three types of variables are included: Background and demographic variables (maternal education, disability group, parent stress, and medical/health status), predictor variables (pretest status and intervention), and outcome variables. All variables are clearly defined and operationalized. The choice and definition of variables is appropriate for the study and represents a well thought out, comprehensive approach to the determinants of developmental outcome. The only exception is for the child medical/health status variables, all of which are based on maternal interview, raising the question of how accurate this information will be.

The hypotheses are carefully elaborated and clearly derived from the literature review and preliminary work done by the investigators. A complex set of interrelationships is postulated, with direct and indirect paths between demographic/background predictors, pretest status, intervention, and followup outcome. These associations are well documented and justified. Moreover, the effects of the intervention are not only examined as a function of exposure (yes/no), but also as a function of the amount of intervention received.

The assessments to be used in the proposed study are well described in terms of their psychometric properties and relevance to the purpose of the study. A major portion of the data has already been collected, but the same measures will be used to ensure comparability and continuity of findings.

If there is any flaw in the proposed study, it is the study design. Although two groups are being compared (intervention/no intervention), the two groups are historically determined. The group without intervention was recruited and assessed prior to the development and implementation of the intervention program. Thus, no random assignment was possible.

However, although the present design is not ideal, it is appropriate if (1) the subject characteristics do not differ between the group that received intervention and the group that did not, and (2) the testing conditions under which the outcome assessments are obtained are the same for both groups, and the examiner is kept blind. According to the investigators, both conditions are met; however, clearer documentation of these aspects of the study design would be beneficial.

Given the attention paid to other aspects of the proposal, the population description is sketchy. No information is provided on the children's gender, age, race, socioeconomic status, birth order, etc. There might be other important background variables that interact with the intervention and affect outcome. The samples have been recruited and assessed and, thus, the families of those infants who received intervention need to be contacted for the administration of outcome measures. The investigators have been able to contact 110 out of 126 subjects and have assured their participation. The sample size is well justified in terms of the proposed multivariate techniques to be used and the power analysis.

Attrition is addressed, with causes identified. Arguments are presented as to why the 12 percent attrition experienced will not continue Steps to prevent further loss of subjects are identified. Statistical power is addressed. However, if more than 10 subjects are lost over the next 2 years (a 10 percent attrition rate), the power level would be unacceptably low. The subjects are already 4–5 years of age (somewhat old for preschool assessment, unless they are profoundly developmentally delayed).

The plans for data analyses are described throughout the proposal, and are directly related to the main issues to be addressed—the effects of intervention as a function of exposure (yes/no) and amount of intervention received. In addition, the interactive effects of background variables and infant preintervention status are also assessed.

The time schedule presented lacks detail which would have helped the reviewers understand data collection activities. It is not clear what data collection will occur in the two interviews within 1 month, or when the preschool measurements will be done. The investigators state that they have recontacted the sample and updated their lists of names and addresses, and have only one research assistant to hire and train. Procedures for data collection are already in place. Thus, it is difficult to comprehend the request for a 3-month startup time; this could probably be reduced. In addition, data analyses for a sample of 110 should not require 9 months, since some analyses can be done after 6 months of data collection.

A SELF-MANAGEMENT EDUCATIONAL PROGRAM FOR SEVERELY ASTHMATIC CHILDREN

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PROJECT NUMBER MCJ-350594

PROJECT PERIOD 05/01/90–04/30/93

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	141,328	140,337	148,757	n/a	n/a
Requested	164,757	165,102	175,009	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

Children with moderately severe to severe asthma represent a significant population of children with special health needs. The Children's Medical Services of New Mexico (CMS) and the University of New Mexico Pediatric Pulmonary Center (UNM-PPC) have determined that the major problems faced by asthmatic children and their families in New Mexico are the need for financial coverage for specialized medical care, and the need for education in self-management and self-monitoring techniques. In addition, because of distances traveled, there is a need for followup in the patients' rural communities, which requires education of local health care providers. Because of the State's predominantly rural nature and significant Hispanic and American Indian populations, New Mexico is an ideal model for testing effective methods of rural case management, educational programs adapted to family needs, and effective collaboration in delivery of tertiary-primary care.

Thus, this study addresses the problem of managing moderate to severe childhood asthma in this rural, highly ethnic population. Specifically, this project evaluates systems of providing case management for families of asthmatic children, and has developed and is testing educational and medical intervention through tertiary-primary (community) collaboration in health care. The desired outcome is to reduce morbidity and enhance adaptation for children with moderately severe to severe asthma.

Research Questions or Hypotheses

This study addresses the following question: Do a comprehensive medical program and educational self-management program have an impact on asthma morbidity, cost of medical care, and family stress among children with asthma who live in rural communities? In order to address this question, two groups of asthmatic children are studied. One group receives comprehensive medical care (CMC) consistent with "Guidelines for the Diagnosis and Treatment of Asthma" (National Heart, Lung, and Blood Institute, 1991). The other group receives the same comprehensive medical care, but also receives a structured self-management educational program (CMC-Plus). All subjects have moderately severe to severe asthma, are from low-income families, and live in rural communities.

This study tests the following hypotheses: Provision of CMC-Plus, compared to CMC alone, will (1) reduce asthma morbidity, as indicated by decreased emergency room visits, hospitalizations, and daily symptoms, and by improved pulmonary function parameters; (2) reduce costs of hospitalization and emergency room visits, but not costs of providing asthma services overall; (3) reduce family stress, as measured by the Parenting Stress Index; (4) enhance self-management and self-efficacy as measured by self-report on a structured interview; and (5) enhance self-reported satisfaction with delivery of asthma-related health care services, at both tertiary and primary care areas.

Study Design and Methods

The New Mexico Asthma Project uses a randomized block design with random assignment of subjects by county into one of two treatment groups: comprehensive medical care (CMC) and comprehensive medical care plus a structured self-management educational program (CMC-Plus). Patients in the CMC-Plus group also receive part of their asthma education program via phone followup at intervals during the 2-year followup period. The University of New Mexico School of Medicine Pediatric Pulmonary Center and the local primary care physician jointly provide followup for patients in both groups. Complete transfer of care of the patient to the primary care physician occurs at the end of the project. Identification, referral, and followup of cases are conducted by Children's Medical Services case managers.

Educational intervention for the two groups is as follows: For the CMC group, families receive standard written and verbal instructions on dosage and administration of medication, side effects, and use in acute symptom management. The nurse specialist conducts this educational intervention with individual families at each clinic visit.

Self-management education for the CMC-Plus treatment group is the Open Airways/Respiro Albierto program, which is adapted for use in this rural population, using grouped educational sessions. This six-session program uses problem-solving and decision-making techniques with group interaction. Two of the sessions are provided at the initial clinic visit, two at the 1-month visit, and two are adapted for telephone use during the telephone intervention at 2 and 4 months.

The nurse specialist places followup telephone calls to the CMC-Plus group at regular intervals to determine whether problems have arisen, to obtain peak flow meter readings, and to provide self-management education.

Data are obtained in four major areas: Physical status, acute asthma management, cost of care, and family adaptation and parent satisfaction. Physical status measurements include baseline and periodic followup medical examinations. Data from the history and physical evaluations are collected on forms developed specifically for this study and adapted from standard pediatric pulmonary history and physical formats. Pulmonary function testing includes standard spirometry, peak flow measurements, and bronchoprovocation studies by methacholine challenge which are performed at entry into the study, at 1 year, and at 2 years to determine the degree of airway hyperreactivity. Spirometry is performed at each clinic visit and peak flow monitoring data are collected 2 weeks before each clinic visit.

Data on acute asthma episodes (hospitalizations, emergency room visits, and physician's office acute asthma visits) are obtained through three mechanisms: (1) Diary cards indicating symptoms; (2) documentation by Children's Medical Services case managers; and (3) self-report by parents and children, using the New Mexico Asthma Project Basic Questionnaire, an adaptation of the Open Airways Needs Assessment and Evaluation Interview. Cost of care is determined using computerized reimbursement data from Children's Medical Services.

Family adaptation is determined by several self-report questionnaires, including the Parenting Stress Index (PSI), a 120-item self-report measure that evaluates stress related to child rearing or to dysfunctional parenting. Three main domains of stressors are identified and evaluated by the PSI. The Family Rating of Care Scale determines parent satisfaction with the program.

Population Description and Sampling Plan

The population for this study is drawn from rural, highly ethnic counties throughout the entire State (excluding the urban county of Bernalillo). Subjects must meet CMS economic and asthma-severity criteria. Counties have been matched for population, ethnic distribution, and health manpower for allocation to treatment groups. Children range in age from 2 to 18 years and must have moderately severe to severe asthma.

All sample size calculations are based on findings from the New Mexico Asthma Project pilot studies in six rural counties in New Mexico. Based on pilot data, 125 patients are being entered in each group to assure an adequate sample size at the end of 2 years, given a 20 percent dropout rate. Sample size calculations are based on the number of hospitalizations for asthma in 6 months, number of emergency room visits in 6 months, number of days in the hospital for asthma, number of school days missed, and the results of the Parenting Stress Index. Based on pilot data, it is estimated that the study population will be approximately 60 percent Hispanic, 10 percent Native American, and 30 percent non-Hispanic white.

Analysis Plan

Data from questionnaires, diary cards, pulmonary testing, and acute/primary care usage are entered and stored, using a relational data base management program. Data entry is performed by the data management specialist, and the project coordinator checks for accuracy by random verification. Descriptive statistics from the individual subject data files are analyzed, using currently available software programs, such as Paradox. Further analysis of the data is performed using the SAS statistical package on a personal computer. Data are formatted from the data management files to the format compatible with SAS, using a commercially available program. This prevents the risk of incorrect transfer of data inherent in repeated data entry. The appropriate statistical analysis is a two-way analysis of variance (if assumptions of quality of variances and normality are satisfied), followed by the Neuman-Keuls multiple comparison test for detecting any pair-wise differences between the groups. If the assumptions for two-way analysis of variance are not satisfied, appropriate transformation of the data is done or nonparametric procedures are performed. Adjustment for ethnicity and age is made during the analysis. If an interaction of these variables with treatment group is observed, the analysis will be conducted separately within each ethnic or age group. If distributions are different, data will be analyzed within blocks.

PRE-AWARD EVALUATION

Originality and Importance

This is an original proposal to rigorously test the success of a health care program for children with moderately severe to severe asthma in a rural, highly ethnic population in New Mexico. Asthma is a leading cause of morbidity in childhood, affecting over 2.2 million children under 17 years of age. According to the application, there has been a pattern of increasing severity, morbidity, and mortality over the last several decades. Asthma can have a major impact on children and their families, and recent advances in medical care and self-care education programs have not been used extensively outside major urban areas.

Regional and National Significance

This study is important and could be applicable to other health care issues as well as to asthma. The success of the program in rural areas with the Hispanic population in New Mexico would have implications for similar populations outside New Mexico. Consequently, the study has both regional and national significance.

Scientific and Technical Merit

This is a well-written, concise proposal. The problem is clearly stated and the need for the proposed clinical trial is supported by pilot data from six counties in New Mexico. The pilot data confirm that there are significant numbers of children from rural, predominantly Hispanic populations who have asthma and need comprehensive services. The literature review seems to be complete, current, and pertinent to the research problem being studied. A good case is made that those asthma self-management education (ASME) programs which have been based on sound behavioral science principles and have been tested using randomized control designs have demonstrated effects such as decreased hospitalizations, emergency room visits, and frequency of attacks. School attendance and grades also have improved, and asthma management skills have been enhanced. All of these effective programs emphasize behavioral techniques such as active involvement, goal setting, and social reinforcement as learning strategies. The basic curriculum in all programs includes: (1) Anticipation of asthma management problems; (2) determination of appropriate responses to problems; and (3) practice of behaviors that result in effective solutions. All programs emphasize better partnership with the physician, which should be achieved as the family becomes more informed and active in management. The program selected for the present study is Open Airways, which has been used with low-income and low-education inner-city families. It is available in Spanish. For some populations, the program also may involve cost savings. Overall, there is an excellent practical and theoretical framework supporting the study.

Other aspects of the proposal are clearly described, such as the explanation of concepts and working definitions of moderately severe to severe asthma. Five hypotheses have been developed to compare the CMC and CMC-Plus groups. Parents and children will evaluate the program. Choice of instruments and variables for assessing the relevant parameters, including measurement of physical status and acute asthma episodes, are described and appear to be appropriate.

The choice of a randomized controlled study design is excellent. The principal investigator appears to have a well-described and appropriate plan for implementing the design, for providing followup of children enrolled, and for coordinating management aspects of the program. The principal investigator is also cognizant of the difficulties of implementing the ASME programs, particularly in rural communities; she has developed realistic estimates of the personnel efforts needed to recruit and retain both families and community physicians for this study. Attrition may be about 20 percent, but sample sizes may still be sufficient, based on the statistical power calculations that have been made. The investigator plans a minimum of 100 subjects per group.

Counties have been matched for population, ethnic distribution, and health manpower for allocation to treatment groups—this is an important analytic point that was not mentioned in the analysis plan. This means that the unit of analysis is not the individual child or family but, rather, the county itself. Children/treatments will be nested within a county, and the investigator needs to account for this important design feature in the analyses and power calculations. So, while two-way analyses of variance can be done, they need to be more sophisticated to incorporate these nesting and experimental unit considerations. Whether it is approximately correct simply to use the child as the unit of analysis will depend on the degree of clustering within counties that occurs in the data. Adjustments for ethnicity and age can still be made during the analysis, as proposed.

The plan for using a laptop computer to enter interview data directly is a good one. The choice of a relational data base management system and SAS on a personal computer will also facilitate analysis of the study results. The timetable seems appropriate, and it appears that the study has not been submitted elsewhere.

The investigator's submission to the Institutional Review Board includes the information needed in order to judge the risk to subjects. However, the consent form is inadequate because it does not inform subjects about the project and any additional expectations beyond the questionnaires, nor does it explain that their doctors will release information to the investigators, and that their refusal to participate will not jeopardize their care. The form does not contain a specific statement for subject families who do not speak English.

The budget is reasonable, but it elicits a few questions. No explanation is given for requesting funds for a color monitor to be used with the computer. In addition, the amount requested for computer software and maintenance appears to be a bit high, and no details are provided about the costs and maintenance of the software packages.

YOUNG ADULT USERS OF SERVICES FOR CHILDREN WITH SPECIAL HEALTH CARE NEEDS: SERVICE UTILIZATION, PSYCHOLOGICAL STATUS, AND DEVELOPMENT TASKS

GRANTEE Johns Hopkins University

INVESTIGATOR

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PROJECT NUMBER MCJ-360578

PROJECT PERIOD 10/01/89–09/30/91

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	239,888	115,790	n/a	n/a	n/a
Requested	247,128	66,509	n/a	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

Older adolescents and young adults with serious physical health conditions encounter substantial difficulties in making the transition from pediatric programs to adult services. Although anecdotal reports from several tertiary care centers describe some of the problems, State and national data on this population are scarce. This information is especially relevant to State programs for Children with Special Health Needs (CSHN) because they discharge participants at age 21 with little specific knowledge of their subsequent needs or problems. This study addresses the problem through a cross-sectional survey of 1,200 older adolescents and young adults who are currently enrolled in, or have been recently discharged from, State CSHN programs. The study fills critical gaps in knowledge about this population by describing the sample on a broad range of variables and by identifying risk factors for lack of medical care, high rates of psychological symptoms, and difficulties in achieving appropriate developmental tasks.

Research Questions or Hypotheses

This study's goals are to:

1. Describe the sample group (in each State and in total) with respect to demographic and health-related variables, patterns in the use of health care

services, rates of psychological problems, and achievement of developmental tasks;

2. Identify demographic and illness-related characteristics that increase risk for (a) lack of a regular source of care, (b) psychological symptoms and lower self-esteem, and (c) problems in achieving appropriate developmental tasks;
3. Test the specific hypothesis that respondents' perceptions of the impact of their condition on their lives mediate the effect of condition-related variables (such as functional severity) on mental health; and
4. Specify the relationship between enrollment status and patterns of health care utilization and insurance coverage.

Study Design and Methods

This study is a cross-sectional telephone survey of 425 individuals born between 1966 and 1970 (inclusive) who were active cases of two State CSHN programs (Illinois and Ohio) at the time of their 18th birthday. The study population ranges from 19 to 24 years of age. Potential respondents were randomly sampled by age cohort from the State CSHN computer records. Within each State, the total age cohorts are roughly comparable in size. Potential study participants were excluded if they (1) claimed no serious ongoing physical health condition at age 18, (2) denied receiving any support from the State CSHN agency at any time, (3) were found to be deceased, (4) were in a residential institution, or (5) were living out-of-State. It was impossible to draw samples from additional States with large populations of individuals 18–21 years of age, due to poor data management systems in State CSHN programs. (Data management problems included nonautomated data files, gaps in data that preclude patient tracking, high error rates in data collected, lack of systematic updating of information, and extremely poor central control of information from local agencies.) Information about the steps taken to develop samples from additional States may be obtained from the principal investigator.

The study uses a 45-minute structured interview. To permit comparisons between study subjects and healthy populations of the same age and demographic characteristics, many of the items in the interview have been derived from existing surveys, such as the National Health Interview Survey (NHIS). The survey included standard scales such as Rosenberg's Self-Esteem Scale, Ilfeld's Psychiatric Symptom Inventory, and a new scale to assess perceived impact of condition on developmental tasks.

Population Description and Sampling Plan

The sample reported a wide range of chronic conditions, including heart conditions, major sensory limitations, orthopedic problems, birth defects (including spina bifida and limb deformities), and medical diagnoses such as asthma, diabetes, and hemophilia. The majority of the sample (62 percent) reported only one condition; approximately 26 percent reported two conditions; the remaining 12 percent reported from three to six conditions. The sample is evenly split between males and females in both States, across the cohorts, and in the full sample. Of the completed interviews, 33 percent were obtained from proxy respondents. The percentage of proxy respondents is roughly similar in both States and across cohorts.

Overall, the majority (78 percent) of respondents are white; 69 percent of the respondents are not receiving welfare or Medicaid payments, and 68 percent are not receiving Supplemental Security Income (SSI) payments. In comparison to the Ohio sample, respondents from Illinois are more likely to be black (21 percent compared to 13 percent from Ohio), more likely to be on welfare or Medicaid (31 percent compared to 26 percent), and more likely to receive SSI (38 percent compared to 26 percent).

Few differences exist on these variables among the four youngest cohorts; in comparison, the oldest cohort (i.e., the 1966 cohort) is more likely to be black, to be on welfare or Medicaid, and to be receiving SSI payments. The oldest cohort also is less likely to have completed high school (39 percent of this cohort report completing the 12th grade, compared to more than 50 percent for other cohorts). The cohorts do not differ in the percentage of respondents who have completed grades beyond high school. Most of the respondents are not married but, as expected, the percentage of married respondents increases in the older cohorts. Respondents report that approximately 44 percent of mothers and 39 percent of fathers have a high school diploma, and about 18 percent of mothers and 13 percent of fathers have completed grades beyond high school. There are only minor differences in these variables between States and among cohorts.

Analysis Plan

To accomplish the research goals, the study conducts the following analyses:

Goal 1: Describing the population. We calculate absolute values and percentages of the sample on a wide range of variables, including visibility of illness, age of onset, course of illness, limitation of activity, self-esteem, and psychological symptoms.

Goal 2: Identifying factors associated individually or in combination with inadequate medical care, higher scores on measures of psychological distress, and problems in achieving developmental tasks: First, we complete *t* tests and analyses of variance to identify significant bivariate relationships; subsequently, we use multiple regression procedures to determine potential direct and interacting effects when key variables are considered together.

Goal 3: Testing specific hypotheses regarding the mediating role of perceived impact on the relationship between condition-related variables and mental health status: We use a strategic series of multiple regressions.

Goal 4: Specifying the relationship between enrollment status and health care use: We perform chi-squared tests of the association between enrollment status and presence of a regular source of health care, insurance coverage, and frequency of service utilization, accounting for potential differences in key variables between the enrolled and discharged groups.

PRE-AWARD EVALUATION

Originality and Importance

This proposal seeks to characterize accessibility and use of health care services, education and employment status, and social and psychological adjustment in young adults who have recently been, or are about to be, discharged from State CSHN programs due to their age. In addition, the study seeks to identify needed but unavailable services; to identify subgroups at high risk for lower educational/vocational attainment, impaired social relationships, and increased rates of psychological distress; and to provide information to CSHN programs to respond to these needs. Such a study would carry great weight in policy formulation and planning at both State and national levels, and its findings could lead to improvement in the quality of life for handicapped young adults and to reduction in the social costs of integrating these individuals into the larger society. The proposed research is congruent with MCH/CSHN programmatic goals.

Regional and National Significance

This proposal has national scope and would affect communities of all sizes throughout the Nation. The study areas are geographically diverse and would yield information on regional variations in the level of services provided as well as the degree of unmet needs. Despite the longevity of the CSHN program, there are few multistate studies of the structure and financing of these programs and the services provided, their effect on health care for children, and the population that uses these services. The current investigation would partially fill this gap.

Scientific and Technical Merit

This application is a revised version of one reviewed earlier and approved but not funded. The reviewers felt that the investigators had responded to most issues raised in the prior review, but still felt the budget was greater than warranted. Some new issues were raised, such as the failure to specify the exact nature of some of the variables.

The problem is stated clearly and its relevance to State CSHN programs (and to other programs and projects) is reviewed. The pertinent literature is reviewed in detail, beginning with national CSHN programs, followed by indepth discussion of a conceptual model of the developmental transition from adolescence to young adulthood. The literature pertaining to the effects of chronic illness on this transition is also reviewed. The rationale for using a multifactorial and noncategorical approach is defended. The entire discussion presents a plausible framework for the research.

The conceptual framework for the study is well thought out. In particular, the concept of the "career path" of services used during transition from adolescence to adulthood is a helpful unifying concept. The study's apparent strengths include an emphasis on societal and developmental stresses (in addition to the purely medical and psychological attributes of chronic illness) and the treatment of various disorders as different manifestations of chronic illness. The investigators argue convincingly for understanding the responses to the various problems experienced by this population of young adults in the context of a developmental perspective, assessing progress in their ability to move toward independence, identity consolidation, interpersonal relationships, and adult roles. This perspective provides a solid framework for the proposed assessment.

Because the population of interest is not currently understood even in such basic terms as demographic characteristics, gender, poverty status, race and ethnicity, source of insurance (if any), distribution of diagnosis, course of illness, age at onset, health care availability and utilization, psychological adjustment, education, and vocation, these and other descriptive indicators will be examined and described. This purely descriptive stage is a necessary first step.

The second goal, further specified in this proposal, should help to identify subgroups of individuals at high risk for adverse outcomes. This is an important aspect of the study, since it is likely that this kind of information would offer the most specific help to State health programs in identifying those young persons about to be discharged who need extended programming to make the transition successfully.

With respect to the third goal, the analysis includes reasonable steps that should allow assessment of relationships between disenrollment and patterns of health care utilization and insurance coverage, accounting for age, diagnosis, and other variable factors. The time since disenrollment will be the main independent variable in the analysis. The analysis will depend upon the sample available. As the investigators recognize, a full assessment of disenrollment would require a longitudinal design.

The investigator has provided a good response to previous criticism of the study's timeframe and resource requirements. The study period has been reduced from 36 to 18 months, and the cost has decreased proportionately by approximately 50 percent. The present timeline seems appropriate and all resources are well justified and appropriate.

There are still problems. The measures to be used are described, but it is unfortunate that the investigators felt it was sufficient to state that the validity and reliability of the instruments have been established. This is a matter of interpretation that should have been left to the reviewers of the proposal. In most cases, details are provided about reliability but not validity.

The proposal does not provide any demographic description of the individuals on the roster of each of the two States. It would have been helpful to know if there were any gross differences in level of socioeconomic status, race, age, or percentage of each handicap. If large differences exist, a case could be made for performing some analyses separately for each State.

The internal review board at Albert Einstein College of Medicine has given approval. Participant consent will be verbal after the subject has received and supposedly read a letter describing the study. The first telephone call will verify the subject's consent and then schedule a time for the interview. During this telephone call, the study will be reviewed verbally. The sample script includes the opportunity for the subject to ask questions. However, no actual statement is obtained from the subjects that they are, in fact, willing to participate. It seems important to add this confirmation to the script. The investigator has not addressed previous concerns about how subjects are approached. It is not clear who would conduct the mailings. Those who refuse to participate will still be asked for demographic information; it seems important to give them the option of deciding whether or not to participate, even on this limited basis.

IMPROVED PRENATAL DETECTION OF THE FRAGILE X SYNDROME

GRANTEE Research Foundation for Mental Hygiene, Inc.

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PROJECT NUMBER MCJ-360587

PROJECT PERIOD 10/01/89–09/30/94

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	99,261	113,906	114,871	117,292	
Requested	99,261	113,906	114,871	117,292	

* Indirect included

SUMMARY

Statement of the Problem

Fragile X syndrome is the most prevalent inherited form of mental retardation. This syndrome has been found to occur in all racial groups, and affected children are usually moderately to severely retarded. Although it can be detected by prenatal testing, prenatal diagnosis is not yet widely available because the testing is technically difficult and is not 100 percent reliable.

In 1981, we reported the feasibility of the primary prevention of this disorder through prenatal detection. It is estimated that more than 1,000 trials have been conducted worldwide, and at least 111 cases of prenatal fragile X diagnosis have been reported in amniotic fluid (AF), fetal blood or peripheral umbilical blood (PUBS), and chorionic villus sample (CVS) cultures. Most of the prenatal fragile X trials to date have been made using AF, because amniocentesis has been by far the most widely available and lowest risk prenatal test. It is estimated that fragile X detection in AF is about 90 percent reliable with regard to false negatives and nearly 100 percent reliable with regard to false positives. False negative results have been reported in all three types of protocol (AF, CVS, and PUBS). Because of these limitations in reliability, prenatal fragile X testing is still regarded as a research or experimental procedure; thus, a number of laboratories will not offer this test to pregnant women who are obligate carriers of the mutation. A more rational explanation for some or most of these false negative results is needed. This project investigates and develops new procedures that will reduce or eliminate this problem and thereby improve the prenatal detection of fragile X syndrome.

Research Questions or Hypotheses

The goal of this study is to improve the reliability of the prenatal detection of the fragile X chromosome in AF and CVS by studying known variables as well as improving or developing new protocols, and incorporating new information as it becomes available during the course of the project. We expect that improvements in the detection of both the fragile X or marker X chromosome as well as the fragile X mutation, recently referred to as FMR-1, will be made and/or developed for incorporation into this project.

Study Design and Methods

Prenatal fragile X detection studies are carried out primarily in CVS and AF cultures obtained from pregnant women at increased risk for having a fetus with the fragile X syndrome. Variations in the type of culture media used as well as the type of fragile X induction system are studied to determine whether an optimal set of conditions can be identified for detection of the fragile X chromosome. For example, we have established that fragile X chromosome induction is not possible in Chang medium, a tissue culture medium that allows rapid cell attachment and growth. We have determined recently, however, that Chang medium may be employed initially in combination with another medium, followed by a specific time of "recovery" in the second medium before attempting fragile X induction.

We have also determined recently the prevalence of a fragile site that could be confused with that of the rare fragile site that characterizes fragile X syndrome. In addition, we have helped to establish that a combination of fragile X induction systems is necessary for optimal detection of the fragile X chromosome. In some cases, one induction system may work well, while with others it may not be effective. Through SV40 transformation, we have also transformed a number of AF or CF fragile X positive cell cultures, which can now be used as positive controls or for further research on the FMR-1 mutation in prenatal material. In addition, where possible, families have been offered DNA linkage studies to further improve the reliability of both maternal carrier and prenatal detection.

In light of recent molecular breakthroughs, including identification and cloning of the fragile X mutation during the past year, we have embarked upon a validation study of prenatal fragile X detection using both direct DNA and polymerase chain reaction (PCR) technology in parallel with cytogenetic testing. In 21 prospective trials thus far, we have had no false positives or negatives and have identified correctly the status of the mutation in 5 positive fetuses with the full mutation and in 1 transmitting male with a premutation. In addition, during this time period, at least nine cases were successfully tested retrospectively from frozen samples preidentified cytogenetically.

We were the first group to report in the literature retrospective FMR-1 detection in AF cultures and we provided cytogenetic control data for the first report in CVS cultures. Our work continues in an effort to further optimize the PCR method of prenatal fragile X detection together with selective parallel cytogenetic and direct DNA confirmation studies. Thus far, we have experienced cases where prenatal detection turn-around time has been reduced from 3–5 weeks (for cytogenetics) to 3 days (using PCR technology).

Population Description and Sampling Plan

Testing is carried out on samples referred to our center. These referrals (usually from within the United States but occasionally from Canada, Europe, the Middle East, and Far East) have been increasing, with the biggest jump occurring during 1991, probably because of the availability of direct DNA testing for the fragile X mutation itself. It is clear that utilization of prenatal fragile X detection is increasing, and with the optimization of PCR testing and simultaneous reliability (sensitivity) improvement to virtually 100 percent, the test will be utilized on a much wider basis.

Analysis Plan

As validation of direct DNA and PCR testing together with cytogenetic analysis proceeds, both false positive and false negative results are tabulated together with all other results. A reliability value will be calculated, as the number of trials proceeds in relation to both false negative and false positive results. At the present time, reliability for cytogenetically positive results is nearly 100 percent. Reliability in our laboratory with regard to false negatives is nearly 97 percent, while it is considerably less than that worldwide. In addition, when evaluating whether improvements occur within or across particular cytogenetic or molecular protocols, appropriate statistical analyses will be used, including *t* tests, chi-square analyses, and analyses of variance.

PRE-AWARD EVALUATION

Originality and Importance

Few laboratories are currently offering fragile X screening of their genetic specimens because of the difficulty in inducing the fragile X changes and concern over false negative results. If the investigators are able to improve the specificity of the culturing techniques and to provide positive controls through SV40 transformation, then testing is likely to become much more widely available.

Regional and National Significance

The frequency of this disorder is similar to that of Down syndrome, is more difficult to diagnose clinically and cytogenetically, is known to be present in all populations that have been tested to date, and can result in mental retardation more severe than in Down syndrome. It presents an enormous public health problem of great significance.

Scientific and Technical Merit

This application is a revision of a proposal that was previously submitted but not approved. The review of the literature is adequate, up-to-date, and provides enough information to allow one to conclude that the proposal is a logical and relevant outgrowth of previous studies. The proposed variables and preliminary data are described adequately, although this part of the application is extremely hard to follow.

The investigators provide many letters of agreement from the largest genetics laboratories in the country indicating that the principal investigator's lab will be used as a primary or reference lab for the detection of fragile X, and so it seems likely that the expected number of positive cells will be received. However, it is impossible to tell whether this will be enough to permit identification of the best culture and induction scheme, since performance of the cells under the conditions to be tested is as yet unknown; only experience will demonstrate when the sample size is sufficient. On the other hand, since this is the reference laboratory in the United States for fragile X, there is no more likely candidate for funds to continue this work.

The two-way analysis of variance is the most reasonable approach, as the investigators suggest. Power calculations are not practical, since baseline incidences of fragile X induction are as yet unknown.

EFFECTS AT AGE FIVE OF AN INTERVENTION PROGRAM FOR LOW BIRTHWEIGHT INFANTS

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PROJECT NUMBER MCJ-360593

PROJECT PERIOD 05/01/90–04/30/92

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	275,729	196,962	n/a	n/a	n/a
Requested	275,729	206,684	n/a	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

The primary purpose of this project is to test the premise that early intervention can produce lasting beneficial effects on the incidence of health problems and developmental failures among low birthweight (LBW) children. A second purpose is to collect and provide information on the need for and delivery of special health and education services for low birthweight infants, such as those mandated by P.L. 99-457 for at-risk children during their preschool years.

The Infant Health and Development Program (IHDP) is the first multicenter randomized controlled trial of an intervention consisting of early child development programs and family services for low birthweight infants, a group known to be at high risk for developmental dysfunction and school failure. This trial has the potential to provide pertinent information on national policy matters, particularly on the efficacy of early intervention programs in enhancing cognitive, behavioral, and school-related outcomes of such children. The trial also has implications for the closely related issue of providing services to handicapped and at-risk infants and preschoolers.

Research Questions or Hypotheses

The success of early intervention studies on socioeconomically disadvantaged children provided a rationale for investigating the effectiveness of similar educational and health interventions for children at biological risk, some of whom have the additional problem of social disadvantage. The Infant Health and Development Program has been implemented specifically to test the effectiveness of a comprehensive family support and educational intervention program with high quality pediatric followup. Significant treatment effects have been found at age 3: Low birthweight infants who received the intervention had fewer cognitive deficits and behavior problems than those children who received only high quality pediatric followup.

The current study follows these children through age 5. The study addresses the following specific research questions:

1. What is the nature of the treatment effect, if any, at age 5?
2. Is the treatment effect (if any) at age 5 similar across subgroups defined by maternal, environmental, and child characteristics?
3. Do center-based child care services received in the 2 years following the end of the program influence cognitive and behavioral outcomes, and are these services associated with better outcomes in the treatment group?

The general hypothesis is that this effective preventive strategy through age 3 will continue to benefit children as they enter school, measured in terms of fewer children with low IQ scores, severe behavior problems, neurodevelopmental delays, and deficits that would lead to placement in learning disabled or special education classes.

Study Design and Methods

The Infant Health and Development Program is an eight-site, randomized controlled trial to evaluate the efficacy of an early intervention program for low birthweight children. The intervention provides a comprehensive educational curriculum with family support through three modalities: Home visiting, parent groups, and children's attendance at a child development center program. Infants are randomly assigned to an intervention group that receives all three of these curriculums with additional high quality pediatric followup through age 3, or to a followup group that receives only the pediatric followup. The intervention program was initiated in the intervention group immediately following randomization, upon the infant's discharge from the hospital, and continued until age 3 years corrected age (i.e., age corrected for estimated weeks of prematurity).

The primary functional domains chosen as potential outcomes of the intervention include cognition, language, health, family, behavior, and (later) school readiness. Assessments tapping these outcomes are administered by centrally trained psychologist observers not associated with the past followup of the IHDP families in order to ensure blindness with respect to the children's placement in the intervention treatment group or the followup treatment group. To maintain standardization within and between sites, all observers are supervised by an evaluation coordinator at the site, with overall supervision and monitoring from the Longitudinal Study Office. As in earlier assessments of the children, the measures are obtained in a clinical setting (as opposed to home visits). The measures are as follows:

1. Cognitive development:
    a. Wechsler Preschool and Primary Scale of Intelligence;
    b. Peabody Picture Vocabulary Test-Revised; and
    c. Developmental Test of Visual-Motor Integration.

2. Behavioral competence:
   a. Child Behavior Checklist;
   b. Adaptive Social Behavior Inventory; and
   c. Harter Scale of Perceived Competence.
3. Health status:
   a. Rand General Health Scale; and
   b. Rand Perceived Health Scale.
4. Preschool readiness:
   a. Woodcock-Johnson Psycho-Educational Battery, preschool scale: Subtests for special relations, quantitative concepts, and visual matching.

Population Description and Sampling Plan

Medical schools in eight demographically diverse geographic areas participate in the IHDP: University of Arkansas for Medical Sciences, Albert Einstein College of Medicine of Yeshiva University, Harvard Medical School, University of Miami School of Medicine, University of Pennsylvania, University of Texas Health Science Center at Dallas, University of Washington School of Medicine, and Yale University School of Medicine.

The design includes stratification by the eight sites and two weight groups: Infants weighing 2,001–2,500 grams (designated heavier), and those weighing ≤2,000 grams (designated lighter). Because the lighter group is at greater risk for developmental and health problems, two-thirds of the sample has been allocated to this group. The sample size is large enough to compensate for loss of power due to unequal subgroup sizes and to allow for the possibility of a dropout rate as high as 10 percent per year, or a total of 30 percent through 3 years of age.

Informed consent was sought from the parents of 1,442 eligible infants identified from a pool of 4,551 hospital-born, low birthweight premature infants. Of this group, 305 families (21 percent) refused consent, and the remaining 1,137 families agreed to be randomized. Of the 1,137 randomized, 47 were withdrawn before enrollment, primarily because they either refused group assignment or could not be located. An additional 105 infants, although enrolled in the program, were excluded from the primary analysis group because they were twins of randomized subjects or (in two cases) were cousins being raised in the same household. The remaining 985 infants were designated as the Primary Analysis Group and constitute the cohort for the trial.

Infants were randomized by the National Study Office to either the intervention or followup group immediately after hospital discharge, using a procedure that involves close monitoring for balance and for absence of bias. The characteristics monitored for balance include birthweight, gender, maternal age, maternal education, maternal race (black, Hispanic, and other), primary language in the home, and infant participation in another study.

Analysis Plan

The primary data analyses focus on comparison of the intervention group with the followup group to identify effects that might be attributable to the intervention at ages 4 and 5 in each of the four domains (cognitive development, behavioral competence, health status, and school readiness). All primary analyses are carried out according to original treatment assignment. Children with missing measures are excluded from analyses that require that measure. Initial status characteristics of children with missing measures in the intervention group are compared to those with missing measures in the followup group to assess missing data bias in primary comparisons. Robust statistical methods are used for estimating means (trimmed means are used) and standard deviations (median absolute deviations are used). Stem and leaf charts and letter value displays (five-value summary) are used to explore the primary measures, identify outliers, and suggest transformations of scale, if needed.

Multiple linear regression models are developed for each measure with explanatory variables consisting of treatment group and the following covariates: Birthweight stratum (lighter, heavier), birthweight (measured in grams), site (eight clinics), child's gender, maternal education, maternal age, maternal race (black, Hispanic, other), Neonatal Health Index (an indicator of neonatal health status in the nursery, developed by the IHDP), and interaction terms (as needed) between treatment group and one or more of the above covariates.

Significance levels (*p*-values) for variables in the regression models are based on rank transformations. Nominal significance levels are used; no formal corrections for multiple outcomes or multiple comparisons are made. However, enough information will be given in presented data that corrections such as the Bonferroni's correction could be made.

Many of the primary measures have comparable determinations at two or more ages. Patterns of change from one age to the next in relation to treatment group and other explanatory variables are explored, using techniques of longitudinal data analysis (time series), such as those described by Zeger and Liang.

PRE-AWARD EVALUATION

Originality and Importance

This is an important project that provides a unique opportunity to address a data set and population of immense size. The intervention carried out to date with initial success suggests that an early developmental intervention can have significant benefit for a high-risk population of low birthweight premature infants. Such findings, however, are limited by the fact that followup has only been accomplished through 3 years of age. The overall impact of the intervention can be addressed only by subsequent followup to examine whether the effects last beyond the end of the intervention. This project addresses just these issues by proposing to follow the children up to school age.

Regional and National Significance

This research is clearly of national significance. Not only are eight sites from around the country involved in the intervention and followup, but the problems addressed within the intervention and followup are germane to national problems associated with premature LBW infant followup and service provision programs.

Scientific and Technical Merit

This proposal presents a cogent case for followup of a large population of LBW premature infants that were randomly assigned to an early intervention developmental program, and a group of infants assigned to a control condition in which only followup assessments were provided. The proposal is clear and well written, and the relevant literature is well covered.

The methodology is simple and straightforward. At age 5, children will be seen and assessed with several measures of their cognitive status, behavioral and adaptive functioning, health status, and school readiness. In addition to these measures, other measures are being collected through funding received from various foundations. These additional measures address maternal ratings of health status (occurrence of serious health problems), maternal reports of family functioning and well-being, and families' use of educational, child care, or other special services (measures generated from survey data collected using the format of the National Longitudinal Youth Study).

Overall, the measures to be employed are appropriate to the research questions, and reflect a reasonable approach to assessment of various skills relevant to general developmental functioning and school readiness. In some instances, the assessments involve direct assessments of children's skills; in others, they involve maternal report of child status. It is unfortunate that other independent raters of children's functioning (such as teachers) could not be included in the assessments, but this would add to the already costly nature of the data collection and it is not clear whether all children have attended preschool programs. It would have been helpful, however, if some information had been provided about the reliability and validity of several lesser known measures such as the Rand Perceived Health Scale and the Adaptive Social Behavior Inventory. The approach to data analysis appears sound.

In general, the merit of this proposal rests predominantly with the importance of the followup of this large population. The measurements to be employed are basic, and will add little new information theoretically or empirically to high-risk infant outcome. The question regarding the continued effect of the intervention is important, however, and this investigation is a necessary step in addressing this issue. It is critical to determine whether the effects of the early intervention protocol extend to school age and beyond termination of the intervention. The goal of early intervention is to improve the eventual developmental and academic performance of these children; this research is necessary to achieve the goal and is also important with respect to the continuing controversies about the efficacy of early intervention.

Limitations are evident. These include the potential dropouts or noncompliance that may occur due to cessation of the previously free intervention, and the length (2½ hours) of the proposed battery of tests. In addition, the measures would be taken at one point in time (age 5), so they will be more difficult to evaluate and relate to the effects of the intervention in years 1 through 3.

There is no earlier reference value that would allow evaluation of changes over time. The utility of the information will therefore be limited to a cross-sectional evaluation only.

The budget is extremely large, due predominantly to the multisite nature of the project and the redundancy of personnel needs. The real need for both a study coordinator and evaluation coordinator at each site is questionable. The question also arises as to whether significant economies could be obtained through a more efficient study design, such as using a portion of the eight sites and/or reducing the number of control subjects. Efforts must be exerted to reduce the total funds requested per year, since the budget for this project represents about 70 percent of all funds available to the program to support new research. One possibility is that the grantee institution might forgo a portion of the indirect cost funds if the project is funded.

Although the proposal includes a provision for institutional internal review boards, it does not detail procedures for obtaining informed consent. A copy of the consent letter used at one of the clinics suggests that parents received a supplementary consent letter (the original extended only until the child reached age 3), but more information is needed.

This is a well-written proposal that addresses a research question of great significance for maternal and child health. Unfortunately, the amount of funds required to support the investigation as currently designed is considerably beyond the resources available to the program. The proposal presents no evidence that less costly design alternatives were considered and/or discarded. Deferral is recommended, pending a site visit to discuss design and budget possibilities.

BODY COMPOSITION IN PREGNANT WOMEN

GRANTEE	Columbia University				
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PROJECT NUMBER	MCJ-360601				
PROJECT PERIOD	10/01/90–09/30/93				
COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	356,227	280,451	233,693	n/a	n/a
Requested	404,376	419,464	232,608	n/a	n/a
* Indirect included					

SUMMARY

Statement of the Problem

Studies have shown that maternal prepregnancy weight and pregnancy weight gain are highly associated with infant birthweight in both blacks and whites. However, little has been done to identify the body components that determine these relationships. Recognition of the association of prepregnancy weight and pregnancy weight gain with infant birthweight has had a major influence on Federal policies affecting pregnant women. Billions of dollars are spent each year through the Special Supplemental Food Program for Women, Infants and Children (WIC) to provide additional nutritious food for pregnant women, and eligible expectant mothers are encouraged to apply for food stamps as well. Encouraging adequate weight gain is one of the roles of prenatal care providers. Attitudes toward pregnancy weight gain have been liberalized in the last few years, and in 1988 the National Academy of Sciences Subcommittee on Nutritional Status and Weight Gain During Pregnancy issued new recommendations regarding gestational weight gain that are higher than previous recommendations. A major concern, now that weight restriction is not as widely practiced, is that many women will gain excessive fat, ending pregnancy substantially more obese than before pregnancy. This is a particular concern for black women. About 50 percent of adult black women are obese; yet, because low birthweight and low pregnancy weight gain are more common among blacks, increased weight gain might be desirable.

Further advances in our understanding of the role of weight gain require study of the components gained. Specific body composition changes may contribute to fetal growth as well as to the development and course of maternal disease (including toxemia, diabetes, and obesity). Current knowledge does not permit us to state whether increased fat deposition is necessary for increased fetal growth. It is possible that lean tissue increases (increased body water or plasma volume, for example) are more important, but studies of weight changes alone cannot distinguish these components.

Research Questions or Hypotheses

There are three main questions to be answered by this study:

1. Is greater total weight gain during pregnancy associated with increased fat storage, as it is in nonpregnant subjects?
2. Are maternal fat or lean tissue increments more highly associated with fetal growth?
3. Do racial differences in gestational fat storage occur, and, if so, do they contribute to differences in fetal growth?

Study Design and Methods

This study uses a prospective, repeated measures design to assess body composition and its changes in a sample of 100 black women and 100 white women. The women are recruited, referred to St. Luke's Hospital for the necessary measurements, and followed to maintain participation until after they have delivered. Body composition is measured twice during pregnancy, at 14 and 37 weeks gestation. Measurements include total body water, total body potassium, body density by underwater weighing, extracellular water, bioimpedance analysis, skinfold thicknesses, and anthropometry. At 1 week postpartum, bone density (and fat and lean), by DPX are measured. Our body fat estimate is based on a multicompartment model rather than a two-compartment model, thus improving the fat estimate. This combination of measurements has not previously been applied during pregnancy.

Population Description and Sampling Plan

The subjects are primarily recruited from four sites: Harlem Hospital Clinic, St. Luke's Hospital Clinic, Columbia Presbyterian Hospital Clinic, and the Maternity Center. Participants are 18 to 35 years of age, either black or white by self-designation, nonsmokers, free of major medical illnesses (heart or kidney disease, preexisting diabetes requiring medication, or HIV infection), and first studied between 12 and 16 weeks gestation.

Although the dedication required of the subjects if they are to complete the serial measurement schedule may prevent us from obtaining a perfectly representative sample of the eligible population, the selected group is not expected to differ systematically with respect to body composition, and the usual ethnic differences in fetal growth are expected to obtain in those recruited. Thus, we will be able to appropriately test our hypotheses.

Analysis Plan

Standard descriptive statistics are generated, including frequencies, means, standard deviations, coefficients of variation, and range of response, for the independent and dependent variables. Analysis is preceded by inspection of the univariate distributions of the variables and appropriate partial plots among the variables. Where possible, continuous measures are used to assess all variables (except race). In addition, categorization may be used, depending upon a variable's distributional properties. Further analysis focuses on testing the specified hypotheses.

The hypothesis that higher weight gain is associated with higher fat gain in pregnant black and white adult women is tested by calculating the Pearson correlation coefficient for both ethnic groups and testing the null hypothesis (that the correlation coefficient equals zero) against the one-sided alternative.

The hypothesis that whites store more fat than blacks during pregnancy is examined using analysis of covariance. Fat storage represents the difference in body fat between 14 and 37 weeks gestation. For this test, the null hypothesis is that the average fat store is the same for black and white pregnant women. The covariates used in this analysis include gestation duration, initial body fat, parity, and age.

The hypothesis that fetal growth is greater in white infants than in blacks is studied using analysis of covariance. The covariates are fat gain, initial body fat, height, parity, age, gestation duration, and the baby's sex. The same analysis is repeated using head circumference and birth length as dependent variables.

Models for predicting body fat in pregnant black and white women at 14 and 37 weeks gestation are developed. The independent (predictor) variables considered for model inclusion are: Height, weight, measured skinfolds (triceps, biceps, suprailiac, abdominal, thigh, thoracic, and subscapular), measured limb and trunk circumferences, parity, bioimpedance analysis, and age. Separate models excluding the bioimpedance analysis measurement are also developed for possible use in clinical settings that do not have access to a bioimpedance analyzer. In developing these models, we will consider nonlinear models, interactions, and transformation of the variables. Residual and influence analysis are used to develop and examine the adequacy of the resulting models.

PRE-AWARD EVALUATION

Originality and Importance

Neonatal weight correlates with maternal prepregnancy weight and pregnancy weight gain. White women typically gain more weight during pregnancy and have larger babies than black women. This study seeks to determine racially specific body composition changes with pregnancy. The work is clearly original, although the clinical importance to a non-nutritionist is less justified.

Regional and National Significance

This carefully designed study is likely to produce valid race-specific information. If the noninvasive body composition method (bioimpedance) correlates well with the more invasive measures, this technique could be used clinically.

Scientific and Technical Merit

This proposal has a great deal of scientific and technical merit. The research plan and the proposed methodologies have been carefully evaluated and presented, and the problem is presented in a straightforward fashion. The pertinent literature is reviewed in a balanced manner, key concepts that apply to methodological and design strengths and weaknesses have been considered with care, and the proposed methods utilize state-of-the-art equipment. The populations to be studied will be available to the investigators, and recent experience documents the accessibility of subjects for study, the infrastructure for performing complex field studies in urban settings, and the availability of experienced professional staff to conduct the studies. Preliminary data are presented to document that the majority of the proposed methods can be applied effectively in the target populations. The time schedule is appropriate and a coherent plan for data analysis is presented.

Sample numbers should permit, at minimum, the detection of 1.1–1.6 kilograms difference in body fat with a power of 0.8 and a level of significance of 0.05. Similarly, projected sample sizes should be able to detect a birthweight difference of 160–200 grams between racial groups.

The proposal's major weaknesses are the failure to include sample calculations of body fat and lean body mass and examples of specific approaches that may be used to resolve differences in values predicted by diverse methods. In addition, the plan to define smoking status as anyone who does not smoke after the first 2 months of pregnancy may complicate the interpretation of changes in maternal body composition, and there is only a sketchy explanation of how maternal body weight relative to other parameters of maternal body size will be used in the analysis of relationships between maternal body composition and birthweight.

RISK DETECTION USING OBSERVATIONS OF INTERACTION

GRANTEE	University of North Carolina at Chapel Hill
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PROJECT NUMBER	MCJ-370588
PROJECT PERIOD	10/01/89–09/30/91

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	134,601	125,537	n/a	n/a	n/a
Requested	134,602	125,537	n/a	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

Factors such as adolescent parenting, maternal psychopathology, and preterm birth have been shown to place infants at risk for poor developmental outcomes. Little is known, however, about the manner in which mother-infant interaction patterns may contribute to these poor outcomes, although several studies suggest that these patterns are predictive of subsequent development. This study examines the clinical utility and psychometric properties of an observation system designed to assess mother-infant interaction from birth through the first 2 years of life. This measure, the Greenspan-Lieberman Observation System (GLOS), was developed and field tested at the former Clinical Infant Research Unit at the National Institute of Mental Health (NIMH) for the purpose of describing several critical aspects of the caregiver-infant relationship, especially in dyads at high risk for dysfunctional development. Longitudinal interaction, environmental, and infant development data were collected for 560 mother-infant dyads using standardized procedures at NIMH and at six other sites in North America. These dyads varied with respect to medical and psychosocial characteristics and were followed from birth through the first 2 to 4 years of life. Using this extensive data base, we examine several aspects of reliability, validity, and generalizability of the measure, as well as its clinical utility for risk detection, diagnosis, and treatment planning in maternal and child health care delivery systems.

Research Questions or Hypotheses

The goals are of this study are to (1) demonstrate the clinical utility and quality of measurement in systematic observations to determine how biomedical and psychosocial characteristics of the infant, mother, and caregiving environment interact to produce varied developmental outcomes; and (2) present a refined measure for screening by practitioners in the field.

This study tests the following hypotheses:

1. There exist cohesive subsets of behaviors which reflect several underlying dimensions of the dyadic interaction process and patterns of development in the caregiver-infant relationship.
2. The empirical structure of behaviors reflecting underlying dimensions (as in statistical factors) of dyadic interactions within specific developmental stages of infancy will vary across time as a function of maternal and infant characteristics. At each age, it is expected that the strength and nature of statistical associations among behaviors, as well as mean levels, will differ between normative and high-risk groups. These subsets are useful for summarizing critical aspects of individual and dyadic behavior in risk screening settings.
3. Temporal relationships among interaction summaries (conceptual clusters and empirically derived composites) vary as a function of maternal psychopathology, socioeconomic resources, and the infant's biomedical and developmental status. In more adaptive dyads, greater affection and responsivity during early infancy are expected to be associated with more reciprocity, social initiatives, and dyadic exploration during middle infancy, and with more affection, vocal and behavioral expressions of representational thought and play, and less negativism in toddlerhood. The strength and nature of these relationships are expected to vary in high-risk dyads, depending on the extent of individual and socioenvironmental problems, and whether they receive developmental intervention services.
4. Interactive and developmental competence during infancy and toddlerhood varies as a function of the direct and indirect influences of early biomedical, psychosocial, and interaction characteristics measurable during infancy. Specifically, we hypothesize that a set of observable risk factors can lead to identifying specific aspects of development for dyads who need more extensive assessment and intervention.

Study Design and Methods

This study is descriptive in that it concerns the clinical and psychometric qualities of an observation system. All sites are selected because of the availability of longitudinal data which have been collected using standardized procedures. Most sites have ongoing correlational research in progress and do not conduct intervention studies. Several samples within sites, however, are included because of their involvement in longitudinal experimental and quasi-experimental interventions. These are selected because we are also interested in estimating individual differences as a function of the influence of intervention (rather than treatment effects, which are best evaluated within sites) on interaction patterns across time.

Systematic observation procedures are used to record maternal and infant behavior on the GLOS from videotaped unstructured interaction sessions. All families in the multisite sample are enrolled in longitudinal followup assessment programs, several of which involve direct intervention service provision and/or referrals to community agencies when necessary. All interaction sessions are conducted prior to the developmental exams, according to the individual site's protocol. The mother is asked to "do whatever you usually do with your baby when you're at home together," and the ensuing interaction is videotaped for 10 minutes. Assessment sessions are conducted comparably at each site and data files on all subjects are sent along with videotapes of interaction to the former Clinical Infant Research Unit at NIMH for random assignment to trained observers for coding.

Population Description and Sampling Plan

Because of our interest in risk and handicap detection, we sought study populations which vary greatly with respect to characteristics of infants, mothers, and caregiving environments. We are particularly interested in examining interaction patterns in groups of both healthy dyads and those at risk due to preterm birth, adolescent parenting, and maternal psychopathology, because these at-risk groups constitute approximately 30–35 percent of the annual births and use approximately 70–75 percent of the public health, mental health, and social services in the United States.

The sample populations are followed at six universities and at the NIMH center. They are selected based on their standardized interaction and developmental data collection procedures in studies involving high-risk populations of primary interest for our instrument validation goals. The composition of the multicenter sample is predominantly balanced at each age with respect to the extent of risk factors present.

Analysis Plan

An initial examination of the measure's general discriminant ability is conducted prior to testing more specific hypotheses. We are concerned with whether interaction behavior in the first 2 years of life differs significantly among maternal and infant risk groups. To address this question, data from individual samples are pooled for the particular risk groups of interest: Sick and healthy preterm and full-term infant-mother dyads, adolescent and adult mothers, psychiatrically impaired mothers, chemically dependent mothers, and the normative groups of dyads. A cumulative risk score is calculated based on several psychosocial, economic, and biomedical characteristics of the infant, mother, and caregiving environment. Dyads are then categorized into high (top quartile), moderate, or low (lowest quartile) risk groups, based on their cumulative risk score.

Because of the high percentage of multiproblem dyads and resultant confounds, we examine the cumulative risk by intervention group differences (rather than risk subgroups) initially to determine the discriminant ability of the summary clusters. The dyadic summaries are included as dependent measures in multivariate analysis of variance procedures to test the risk and intervention group main effects and interactions at each age.

In terms of predictive validity, we are concerned with predictive relationships between and among longitudinal assessments of maternal and infant characteristics—namely, to what extent do early GLOS summaries predict later measures of caregiver, infant, and dyadic behavior, and are these patterns consistent within and across risk and treatment groups? Patterns of relationships among the summaries are examined using GLM procedures in which the later scores are regressed on the earlier scores and the cumulative risk, intervention group, and interaction are included as covariates. The strategy for significance testing and followup analyses involves (1) canonical correlation analyses to test overall associations between sets of independent and dependent measures, (2) GLM procedures for assessing unique contributions to prediction, and (3) pairwise comparisons of adjusted group means.

We also examine the ability of the dyadic measures to predict developmental outcome of infants from 1 through 4 years of age. Kent subscales for grouping items from the mental and psychomotor scales of the Bayley Scales of Infant Development are used to summarize cognitive, language, social, gross, and fine motor development. Our hypotheses here concern relationships among subsets of GLOS, Bayley Scales of Infant Development, and McCarthy Scales of Children's Abilities measures. The multivariate analysis of covariance procedures employed to address these issues involve tests of several models. Subscales at 1 and 2 years are treated as separate sets of dependent measures and are regressed on earlier GLOS summaries after covarying the effects of cumulative risk, intervention group, and their interaction.

PRE-AWARD EVALUATION

Originality and Importance

This is a highly original and important project that involves a large-scale, multisite investigation of an observational measure of parent-child interaction applicable to a range of high-risk populations. No other data sets approach such a magnitude with such a diverse set of high-risk samples. The approach taken in the development of GLOS and the constructs involved in this measure are unique, and it offers the opportunity for applicability across a range of potential risk groups. No other observational study of mother-infant interaction in high-risk samples has approached the task from a multisite, large sample size perspective. The ability of the proposed work to address issues previously untestable due to sample size limitations is unique.

Regional and National Significance

This is a project with both regional and national significance. Although the project will be carried out predominantly in North Carolina and Tennessee, it involves the work of numerous investigators from various sites around the country. Furthermore, the principal investigator wishes to include former Clinical Infant Research Unit staff at NIMH who worked on the original and ongoing assessment of GLOS. The at-risk and normal samples are representative of national concerns as well, further indicating the broad significance of the work.

Scientific and Technical Merit

This is a very strong proposal that is well conceptualized and comprehensive with regard to issues of design, measurement, and data analysis. The project involves a unique opportunity to address important substantive questions related to various high-risk populations, early mother-infant interaction, and aspects of children's developmental outcome over time. The large multisite study and data set is a real strength and the availability of differing risk groups for analysis offers unique opportunities to address critically important questions across differing populations.

The major focus of the work to be done involves the study of observed interactions of mother, infant, and dyadic behavior. Furthermore, the GLOS system has been applied to the high-risk sample interactions in a standard way across risk groups, providing comparable data from various sources. The GLOS measure itself has been well developed, and has been tested already for some properties in the infancy and toddler age groups, suggesting that the measure is worth the effort of further establishing its viability and potential utility as a behavioral screening device for mother-infant relationship difficulties.

In general, the proposal is impressive in a number of respects, most clearly for its attention to detail in measurement descriptions, the GLOS descriptions, and the plan for data analyses, which are directly tied to the hypotheses of the investigation. There seems little doubt that this research will add greatly to the knowledge base on mother-infant interactions across risk and nonrisk groups in predicting subsequent mother and infant status.

However, there are several minor problems. First, given the depth of thoughtful measurement in other domains, it was disappointing to find that the outcome measure is primarily from the Bayley Scales of Infant Development. The Kent subscales, which reflect indices of cognition, language, motor, and behavioral development taken from the Bayley Scales, will be the sole measures used. This is an extremely limited and rather disappointing choice, given the complexity of developmental outcome considerations. Perhaps this is the best that could be accomplished across multiple sites, but it is still somewhat unsatisfying, given the otherwise sophisticated measurements applied to the behavior observations and ecological/psychosocial factors which are used to predict outcome.

Second, the principal investigator notes throughout the proposal that data have been collected through age 4 in some of the samples. Further, she states that some of the tapes of mother-child interaction at 30–48 months will be coded as part of the procedures of the proposed research. If this is so, it is surprising to find that data analyses will only be done on the data sets through age 2. It is not clear why analyses of data sets through age 4 will not be done, especially since funds are requested to code these tapes at these ages.

Finally, the assertion that no previous research has addressed biosocial risk and mother-child interactions in the prediction of infant competency is incorrect—there have been several attempts to address such issues, some of which have been previously funded by maternal and child health research monies. This overstatement was truly unnecessary, given the conceptual and methodological strengths of the proposed research, and the ability of the proposed project to address these questions as no previous project has been able to do.

OTITIS MEDIA IN CHILDREN AND LATER LANGUAGE AND LEARNING

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PROJECT NUMBER	MCJ-370599
PROJECT PERIOD	10/01/90–09/30/95

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	281,154	226,372	238,630		
Requested	281,153	292,977	308,604	325,170	336,949

* Indirect included

SUMMARY

Statement of the Problem

Otitis media with effusion (OME), or middle ear disease, is one of the most common illnesses of early childhood, and numerous studies have implicated OME and its associated hearing loss in later speech and language disorders, learning disabilities, and academic problems. Some researchers, however, have criticized the validity of previous studies and claim that no reliable relationship has been identified. This project examines the extent to which OME and its associated hearing loss during early childhood relate to the development of speech, language, intelligence, selected neuropsychological processes, and pre-academic skills during the preschool years. An understanding of the possible association between otitis media in childhood and later development will enable health care providers and educators to be more accurate and aggressive in helping children overcome any disabilities associated with OME.

All children participating in the study are African American and attend day care; 75 percent are from low-income families and 25 percent are from middle-income families. Children from low-income families are at increased risk for poor performance in school, and there is some indication that they are also at increased risk for OME in childhood. In addition, children who attend day care are at increased risk for OME. Determining the extent to which OME affects the development of children attending day care is crucial, given their elevated risk.

Research Questions or Hypotheses

The specific aims of this study are to examine: (1) The relationship between the amount of OME with accompanying hearing loss during infancy and the preschool period and patterns of speech, language, and neuropsychological development during the preschool period; and (2) other factors such as socioeconomic status, gender, quality of the home environment, or type of day care experience which might interact with OME to predict later development of language and learning skills. It is hypothesized that children who experience more days of OME with accompanying hearing loss will score lower on measures of speech, language, intelligence, and attention. Factors such as the child's gender, the mother's educational level, the quality of the home environment, and the quality of the day care environment will influence these relationships.

Study Design and Methods

The middle ear status of the children in the study is monitored every other week by otoscopy and acoustic immittance measures by the medical staff who visit each child's day care center. The diagnosis of OME is established using pneumatic otoscopy in conjunction with acoustic immittance measures. The audiologic assessment consists of age-appropriate pure tone threshold measures (visual reinforcement audiometry, visual reinforcement operant conditioning audiometry, or play audiometry) and speech audiometry. Audiologic assessments are performed in an audiologic test suite in a mobile test van. Age-appropriate threshold measures for pure tones and for speech are obtained four times a year, beginning at the age of 6 months. Threshold tests are also obtained within 1 week of any newly diagnosed OME and at 4, 7, and 13 weeks following the OME diagnosis or until middle ear effusion is resolved. A battery of tests sampling major domains of development is administered between the ages of 1 and 4 years. These domains include speech, language, attention, memory, cognition, and pre-academic skills. The battery consists of standardized and widely used developmental and intellectual tests, language samples, mother-child interactions, and observations in the home and day care.

Population Description and Sampling Plan

A total of 80 African-American children attending day care participate in the study. Children attend one of eight local day care centers in Durham or Chapel Hill, North Carolina. Children identified at birth as biologically normal are selected for the program, enrolled into the research project between 6 and 12 months of age, and then followed through 4 years of age. Half of the children are boys and half are girls. Any African-American child who is less than 12 months old and who attends one of the day care centers is offered the opportunity to participate in the study. The project director informs the parents of these potential subjects about the study. It is estimated that subject attrition will be approximately 10 percent and that loss of subjects should not be systemically associated with OME history, hearing sensitivity, or developmental status.

Analysis Plan

The independent variables of interest index the occurrence and severity of the OME experience and the spectrum of associated hearing loss. The dependent variables are selected measures of developmental domains: Speech, language, intellectual, attentional, and pre-academic skills. Separate analyses are performed to assess the association between OME and development in each domain. Factors such as the child's gender and socioeconomic status, the quality of the home environment, the type of day care experience, and the mother's educational level are likely to be related to performance on these tasks. When significant associations between OME and selected outcomes occur, further analyses are conducted to determine whether the observed association remains significant when these factors are entered as covariates.

The overall goal of this study is to determine whether and to what extent OME is associated with the selected outcome measures. Within each domain, multivariate multiple regressions are performed. Bonferroni corrections are applied within the analyses of these domains to control the alpha rate. Data reduction techniques are applied when the number of dependent measures becomes excessive relative to the sample size. Principal component analyses are used to reduce multiple measures when cross-sectional hypotheses are tested (i.e., dependent measures were collected at a single time point). Multivariate multiple regressions test the association between the outcome measures from a given time period and infant or preschool OME with accompanying hearing loss. Individual growth curves are estimated to describe the development of a characteristic (such as phonological process usage or mean length of utterance). Multivariate repeated measures analyses of variance or nonlinear growth curve analyses test the association between longitudinal outcome measures and OME with accompanying hearing loss.

PRE-AWARD EVALUATION

Originality and Importance

The originality and importance of this study relies not on the main hypothesis to be tested (the association between OME and language and learning) but on the careful documentation of OME, the comprehensive assessment of neurodevelopmental outcome, and the assessment of other factors that might interact with OME in predicting outcome. The potential impact on the understanding and management of OME is significant. The project is not only innovative in the use of a complex theoretical framework and its attention to methodological considerations, but in its significance for the clinical management of a very common childhood illness.

Regional and National Significance

The findings of the study have both regional and national significance, and will be most relevant to black children of low socioeconomic status, a very high-risk population. However, there are two other similar studies being conducted, and, depending upon the population on which they are based, the findings from the proposed study might be redundant. The application presents a clear argument for its relevance to maternal and child health and to the management of OME, including the implementation of screening and referral systems for early intervention at the national level.

Scientific and Technical Merit

This application is a revision of one previously reviewed and disapproved. The problem is clearly stated in terms of scientific as well as clinical significance, and the relevance of the proposed study for maternal and child health is clearly and convincingly presented. The literature review is comprehensive and provides, along with the preliminary studies done by these investigators, the rationale for the proposed study, including the areas of developmental outcome to be assessed.

The main strength of the study design is that it is prospective and longitudinal. The investigators are aware of the limitations as well as the strengths of the design. The concepts and working definitions are provided throughout the proposal and are clearly presented. A simplification of the carefully outlined pattern of associations expected between OME at different ages and different aspects of developmental outcome is represented. The hypotheses are logically derived from the literature review, the investigators' previous work in the area, and the conceptual framework outlined. The investigators pay careful attention to the logical thinking upon which the hypotheses are based.

The proposal describes a very comprehensive set of measures for the audiologic assessment, as well as for the speech, language, and other neuropsychological areas. However, it is still unclear how accurate the assessment of duration of OME will be, based on once-a-week monitoring. The considerable number and overlap of the measures is still not strongly justified. The validity and reliability information still varies considerably from one measure to the other. Some measures are widely used in child development research, while others are more obscure. In general, newer or lesser known measures need more information on their psychometric properties.

The population and sampling plan are well described (except for explaining how an index—which includes measures of family income, parental education, and family stability—will be used to select children). Attrition will be minimal, since the investigators are using the Longitudinal Core Services at the Frank Porter Graham Child Development Center.

The data analysis plan is detailed and very appropriate for the investigation. However, because it takes 2 years for enrollment, the 4-year assessment will not be completed on all subjects within the grant period.

The budget seems high, especially during the first year when only 40 subjects will be enrolled in the study and fewer assessments will be conducted. The estimates for personnel, supplies, and travel should be based on the number of assessments to be conducted every year, and should be considerably smaller in the first year.

The recommendation is for approval with the following conditions: (1) Drop the fourth-year assessment, (2) reduce the budget significantly, (3) submit a power analysis for the proposed sample size, and (4) satisfactorily address the following questions and issues: (a) What are the centers' similarities and differences? (b) The study will depend on parents to have their children treated for OME. What will happen if parents do not take children to a provider to get the needed care? What are the ethical ramifications? (c) Can the duration of OME be accurately determined by once-a-week monitoring? (d) The study was submitted to the National Institutes of Health, as well. What was the outcome of that review?

FECAL COLIFORMS AND THE RISK OF DIARRHEA IN CHILD CARE CENTERS

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PROJECT NUMBER	MCJ-370603
PROJECT PERIOD	10/01/90–09/30/91

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	231,199	n/a	n/a	n/a	n/an/a
Requested	231,199	n/a	n/a	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

The growing use of child care centers for infants and toddlers has resulted in a significant rise in morbidity among children and the individuals who come into contact with them. Acute infectious diarrhea has been found to be 30 percent more common among children attending child care centers than among children who were either homebound or in child care homes. The increased occurrence of diarrheal illness is primarily among children younger than 3 years of age.

Among the organisms most commonly associated with child care center diarrhea outbreaks are *Giardia lamblia, Shigella,* rotavirus, and *Campylobacter jejuni. Salmonella, Clostridium difficile,* cryptosporidium, and hepatitis A have also been reported in child care center outbreaks. All of these organisms share the fecal-oral route of transmission. Studies have suggested that, in addition to increased child-to-child contact, transmission of enteric disease is also enhanced by fecal contamination of environmental surfaces and of the hands of caregivers to whom the children have constant exposure.

At the present time, most State standards for sanitary inspection of child care centers rely on public health department experience in the inspection of restaurants and similar public places. Criteria include water temperature, facilities for sanitary changing and disposing of diapers, and availability of sinks. No direct measures of fecal contamination of the child care environment are used. In this study, we seek to demonstrate that greater fecal contamination in child care centers is related to a higher incidence of diarrhea among children. If this is true, fecal contamination could be used as a measure of the risk of diarrheal disease or as an indicator of compliance with sanitary guidelines or of the success of child care worker training. Gender and ethnicity, among many other sociodemographic characteristics, are addressed in the analysis.

Research Questions or Hypotheses

The study addresses the following hypotheses:

1. The diarrheal disease incidence rates are higher for children in centers with higher levels of fecal contamination than for children in centers with lower levels of fecal contamination, controlling for sociodemographic characteristics;
2. The relative risk of acquiring diarrhea among children attending child care centers varies according to (a) the level of fecal contamination, and (b) the level of observed hygienic practice; and
3. Higher levels of observed hygienic practices in child care centers are associated with lower levels of fecal contamination.

Study Design and Methods

We developed the following instruments for collecting baseline child and family sociodemographic data and center and classroom characteristics data, and for onsite observation of staff hygienic behavior:

1. A child enrollment questionnaire, to be completed by parents, which addresses family socioeconomic status, family size and structure, use of out-of-home child care, and baseline health status characteristics;
2. A center enrollment data instrument, to be completed by the center director, which addresses center size, staffing, and policies;
3. A classroom enrollment data instrument, to be completed by project staff, which addresses staffing and the physical features of infant and toddler classrooms; and
4. A health and hygiene event sampling data instrument, to be completed three times for each participating classroom by project staff, which assesses the child care center staff's diapering and toileting, food handling, and general hygiene techniques by direct observation.

Child care center environments were sampled for fecal coliforms three times at regular intervals during a 7-month period between January and August of 1991. The 10 sites sampled at each center include: Staff hands, child hands, bathroom faucets, bathroom sinks, classroom faucets, classroom sinks, other faucets, other sinks, hard toys, and diapering tables. Samples of surfaces are obtained using premoistened cotton swabs. A sterile template is used to ensure a standardized sampling area. Following sampling, the cotton swab tips are placed in a 2 ml vial of sterile peptone water. After being transported to the laboratory on ice, these vials are vortexed, and the eluted solutions are serially diluted and plated onto MacConkey's agar. Final dilutions evaluated are 1:100 and 1:1,000.

The hands of caregivers and children as well as the toys handled by them are assayed by placing and shaking the objects and rinsing the hands in sterile polyethylene rinse bags containing 200 ml of peptone water. After transporting the rinse bags to the laboratory on ice, a 50 ml sample of the peptone water is concentrated via centrifugation into 5 ml. This 5 ml sample is serially diluted and plated onto MacConkey's agar.

Dilutions of 1:100 to 1:10,000 for toys and 1:100 to 1:100,000 for hands are evaluated. MacConkey plates are incubated at 44°C for 48 hours and then examined. Colonies are considered to be fecal coliforms on the basis of colony formation and lactose fermentation. Suspicious colonies are confirmed as coliforms on the basis of colony formation and lactose fermentation (flat, dry, deep pink colonies) if they are oxidase negative and indole positive. Oxidase positive colonies are rejected as coliforms. Oxidase and indole negative colonies undergo further testing using the API system.

From late January until 2 weeks after the last child care center is sampled (early September), cooperating families are called every other week. The interviews are conducted under contract by Survey Research Associates of Durham, North Carolina, using computer-assisted telephone interview technology. Parents are queried as to whether their child had experienced diarrhea (unusually loose stools) in the preceding 14 days. If so, details regarding the stooling frequency, duration of illness, and other manifestations such as fever, vomiting, and respiratory symptoms are ascertained. On the basis of stool frequency (maximal number of stools during a 24-hour period) and presence of fever or vomiting, each episode is graded from 1 to 4, using the following scale: 1 = minimal (1–2 loose stools); 2 = mild (3–4 loose stools); 3 = moderate (5 or more loose stools, without vomiting or fever); 4 = severe (5 or more loose stools, and either vomiting or fever or both).

Furthermore, in an attempt to differentiate diarrheal illnesses caused by gastrointestinal pathogens from those caused by food intolerances or respiratory pathogens, episodes are categorized as either "pure," meaning only diarrheal symptoms are present without respiratory symptoms, or "both," meaning both diarrheal and respiratory symptoms are reported. Incidence rates are calculated for either "pure diarrhea" (counting only pure episodes) or "any diarrhea" (counting "pure" and "both" episodes). Therefore, all diarrheal episodes are included in the "any diarrheal" rates, regardless of respiratory symptoms. This latter rate corresponds to the rate utilized by prior investigators.

Population Description and Sampling Plan

Computerized lists of licensed child care centers in north central North Carolina are obtained from the State child care office. Lists are ordered in terms of decreasing licensed capacity after eliminating centers with no infants. After obtaining the support of each county's child care information and referral agency, centers are invited to participate in order of size, starting with the largest centers in each county, until the goal of 25 centers is reached. Within each center, one to four classrooms participate in the study, with a preference for two classrooms (one infant and one toddler) per center.

Within each cooperating center, directors and teachers distribute booklets describing the study to parents of children in infant and toddler (up to 24 months of age) classrooms. The booklets contain an informed consent form and a questionnaire requesting baseline information to determine eligibility and to assess sociodemographic status, housing, information on child care use, and other circumstances affecting risk of diarrhea.

Analysis Plan

Incidence density, defined as the number of new episodes per days at risk, is used to estimate the risk of acquiring an infectious diarrheal illness. A new episode is required to be separated from the previous episode by 7 well days. Children are therefore considered to be at risk for a new episode on the eighth day after the end of a previous episode. Because prior studies by other investigators measured attack rate (i.e., the number of new episodes per days under observation, as a measure of cumulative incidence), we also calculate this rate to facilitate comparisons. A third rate, the cumulative illness rate (defined as the number of days ill per days under observation), is calculated in order to estimate the amount of morbidity experienced by child care attendees.

Colony forming units (CFUs) are standardized as follows: Sites with no growth are assumed to have contamination levels midway between zero and the minimal detectable level. Colony numbers that are too numerous to count are assumed to have CFUs twice the maximal detectable level. All sites are sampled in duplicate and CFUs for duplicate plates are averaged. Toy contamination is expressed as CFUs per number of toys sampled. Four toys per rinse bag are sampled whenever possible. The number of CFUs are transformed to $\log_{10}$ (CFU) prior to descriptive or regression analyses.

Multiple regression is used to model the logarithm of the diarrheal rates. The analysis units are three 6–8 week "seasons" for each child care center classroom over the 7-month study. A selection of explanatory variables, within the four data sets listed above, are accomplished by jointly reviewing information from the literature on the past relevance of the variables to diarrheal disease transmission and by examining the strength or lack of correlation between the pairs of variables within each data set. Specific sites of contamination are eliminated if there is little contamination or if the number of sites sampled is seven or less. In addition, a stepwise variable selection algorithm is used to seek predictors of the diarrheal rates.

Initial models for all classrooms are run with classroom age (infant or toddler) forced in. Separate models are then constructed for infant and toddler classrooms, with an allowance for differential diarrheal rates by the three 6–8 week "seasons" during the 7 months of study. Differences in contamination for infant and toddler classrooms at the same child care center are explored by McNemar's test. Results are confirmed using confounders selected by stepwise regression in new models for infant and toddler classrooms.

PRE-AWARD EVALUATION

Originality and Importance

The quest for better means of quality control in infant and toddler child care is an important and unique goal. The magnitude of the problem is well described in the literature review, with incidences as high as 1.24 episodes of diarrhea per child per year of child care. The investigators have shown that these incidences could be reduced considerably and that they interfere with the functioning of the child and the child's family. The proposal is not convincing as to whether the diarrhea problem is a major one or whether it has great economic or public health significance.

Regional and National Significance

The facilities to be sampled are all in Cumberland County, North Carolina. Since there is no evidence that facilities in North Carolina are unique, much of the information should be applicable to child care facilities throughout the United States.

Scientific and Technical Merit

This 1-year proposal builds on an existing SPRANS project entitled "Reduction in Transmission of Infectious Diseases in Child Care Settings" (MCJ-373111). The environmental monitoring procedures that will be used form a major new component of the study. In fact, these procedures and other startup efforts will be pilot tested during the first 3 months (April 1–June 30) of the project year. A stated contribution of this research, compared to previous studies, is that quantitative levels of coliform amounts and microbial contamination will be made. The feasibility of the proposed laboratory methods is hard to judge. The investigators seem to expect little or no problem, but if problems with the sample collection procedures do exist, we do not have much information on alternatives that might be considered. This is a weakness in the present proposal.

Strengths are easy to enumerate. There are three clearly stated hypotheses, which are testable with the proposed research plan. The literature review is concise and relevant, as are the specifications of independent and dependent variables. The application correctly points out that the primary unit of analysis is the child care center itself, rather than the children or teachers, and appropriate measures such as "incidence density" are described for these analysis units. Explanations of concepts and working definitions are appropriate and, as far as can be judged, so are the laboratory collection and processing methods.

The study design is a prospective repeated measure design for environmental sampling of child care center units combined with the prospective cohort study of diarrheal incidence among toddlers and infants attending the child care centers. The impact of the previous SPRANS project on 24 of the 26 centers is not well addressed. Some will have received training previously, some will have just been trained, and two new centers will have had no special training in hygienic practices. These units are clearly heterogeneous, with the possibility of migration of staff among centers. How this affects the data analysis and likely conclusions should be better dealt with in the proposal. More details are needed on this point.

Biases are recognized by the investigators, but methods to reduce them are not discussed in detail. Good compliance is expected from parents and center directors because of the experience of the investigators in the SPRANS project. However, very little detail is given about the preliminary results of that project.

Finally, the data analysis plan is quite complex for sample size considerations but probably appropriate. In contrast, discussion of the analysis pertaining to the primary research questions is elementary.

This 1-year project overlaps somewhat with the existing SPRANS project. There seem to be substantial overlaps in a number of positions. This needs careful review before funding. Also, other reductions should be made. The recommendation is for approval, with a considerably reduced budget.

PSYCHOSOCIAL SEQUELAE OF BRONCHOPULMONARY DYSPLASIA AND VERY LOW BIRTHWEIGHT

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PROJECT NUMBER MCJ-390592

PROJECT PERIOD 10/01/89–09/30/92

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	198,529	184,089	190,034	n/a	n/a
Requested	259,541	269,831	245,139	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

Because of advances in the management of pulmonary pathology and the rapid increase in the survival rate of preterm infants, there are increasing numbers of infants and young children who now survive formerly lethal illnesses, but with the burden of chronic illness or disability. Severe lung diseases, such as bronchopulmonary dysplasia (BPD), are among the most prominent contributors to this increased morbidity.

Infants with severe chronic lung disorders of prematurity are likely to develop a number of negative developmental consequences later in life, including increased incidence of respiratory infections, poor growth, impaired intellectual and social development, and feeding problems. Prospective longitudinal investigations of the course of chronic lung disease and developmental parameters affected by the disease are needed in order to understand the processes underlying later developmental difficulties, and to evaluate intervention strategies which can be implemented in the early stages of illness to ameliorate negative developmental sequelae.

This study focuses on the major cause of severe chronic lung disease in infancy (i.e., bronchopulmonary dysplasia) and examines areas of developmental functioning which could be targeted by potential intervention efforts, such as cognitive and language development, parental stress and depression, and behavioral feeding problems. While the original focus of the project did not specifically include examining social class, race, or ethnic health issues, the dichotomous distribution of the very low birthweight (VLBW) infant population in urban centers has allowed us to focus on how risk factors associated with disadvantaged social class and race may differ, and how access to health care and intervention may differ, based on such factors.

Research Questions or Hypotheses

The study addresses the following hypotheses:

1. Infants with bronchopulmonary dysplasia will exhibit more developmental problems than both a control group of normal-term, healthy infants and a control group of very low birthweight infants without BPD, when assessed on standard measures of growth and intellectual, motor, and language development;
2. Parents of infants with bronchopulmonary dysplasia will show higher degrees of depressive symptomatology and stress than parents of control infants; and
3. Infants with bronchopulmonary dysplasia will exhibit more deviant and maladaptive feeding behaviors than control infants.

Study Design and Methods

This study employs a prospective, longitudinal, quasi-experimental design with measures administered at intake, at 40 weeks, and at 8, 12, and 24 months of age (corrected for prematurity). For all infants, a medical and demographic data base is established, including information on race, sex, gestational age, birthweight, social class, birth order, medical risk, total number of rehospitalizations, total number of days of oxygen dependence, and the presence or absence of specific neurological conditions. All infants are assessed with the Bayley Scales of Infant Development, Hear Kit Screening Assessment, Fagan Test of Infant Intelligence, Sequenced Inventory of Communication Development, and the Child Behavior Checklist. Physical measurements, including measures of stunting and wasting, are also taken.

For parents, the Carolina Parent Support Scale serves as a measure of social support, and the Parenting Stress Index provides some measure of parenting stressors, including ratings of important characteristics of the child, as well as the mother's perception of social isolation and parenting competence. The Beck Depression Inventory and the Brief Symptom Inventory are used as measures of specific distress symptoms, and the Family Environment Scale is used as a means of delineating socioenvironmental characteristics of the family.

All infants are videotaped during a feeding session and these tapes are then scored with the University of Washington School of Nursing Child Assessment Feeding Scale, up to 1 year of age. Mothers are asked to complete a food diary, and a second meal observation is scored based on behavioral observations which quantify number of food acceptances, food avoidance, food refusal, length of meal, number of bites taken, disruptive behaviors, and both negative and positive parental behaviors.

Population Description and Sampling Plan

Subjects are infants with bronchopulmonary dysplasia (for the purpose of this study, defined as oxygen-dependent for more than 28 days following mechanical ventilation during the first week of life, and with persistent increased densities on chest radiographs). The study includes approximately 75 infants with BPD and their caregivers, as well as an equivalent number of very low birthweight comparison infants and term comparison infants, ranging from newborns to 2 years of age. Infants with BPD are expected to remain more chronically ill than the other two groups of infants. The majority of infants are African American. The preterm control group is comprised of very low birthweight infants as closely matched for gestational age and birthweight as possible, who are without respiratory or other severe medical illnesses, and who are on oxygen for less than 14 days. The normal-term control group is comprised of healthy infants greater than 37 weeks gestation who are discharged to home, and spend less than 1 week in the hospital at birth.

Analysis Plan

The overall study design consists of three parts, corresponding to the hypotheses. The first and second parts use a group differences model to assess the effects of chronic lung disease on development, parenting stress, parent-child interaction, and feeding behaviors. These involve comparisons of infants with BPD to VLBW and term infants in the control groups. Because many of the dependent variables are related, formal investigation consists of individual multivariate analyses of variance (MANOVAs), with two factors (group and time). All child developmental outcome measures, as well as parent, family, and teaching measures, are used as dependent variables. To address our second hypothesis, feeding and calorie intake measures serve as dependent variables. MANOVAs with significant overall effect are followed by appropriate posthoc tests.

The major independent variables of the study are lung disease, status, and time; dependent variables are the set of developmental, behavioral, and parental measures outlined above. Control variables include length of stay in hospital, total days on oxygen, medical risk scores, neurologic status, and gestational age. The final component of the design involves only the VLBW infants and assesses the relationship between growth and other outcome variables and a number of biologic, psychological, and social risk factors, using regression models.

PRE-AWARD EVALUATION

Originality and Importance

This proposal is important and original because it fills major gaps in the understanding of growth and development outcomes for infants with BPD. A notable strength is the prospective measurement across domains of inquiry involving development, family, and feeding issues. It seems likely that results from this study could inform intervention with this group of infants and their families in relation to family stresses and adaptations as well as children's growth and development.

Regional and National Significance

Bronchopulmonary dysplasia is affecting a larger number of infants as the survival rate of extremely premature infants improves. Approximately 20,000 infants are affected annually. The illness has an impact on the entire family, and the outcome of these infants is far from ideal. A study that improves our understanding of the problems associated with BPD, especially those that might respond to intervention, would have great value. One can assume that the population to be sampled in this study will be similar to many populations of infants with BPD around the country.

Scientific and Technical Merit

This is a revision of a proposal previously submitted and disapproved. This revised proposal is well written, clearly presented, and attempts to correct or address issues raised in the previous review cycle. In most respects, the revised proposal has been successful in these attempts.

The review of the literature has been expanded and reorganized. It covers logically and extensively areas that are relevant to the current proposal. The strengths noted in the previous reviews remain strengths in the revised investigation plan. The prospective longitudinal design and the careful choice of measurement domains, guided by relevant literature and hypotheses, are particularly valuable and will do much to provide important results useful to both theory and practice. Likewise, dropping the tracheostomy group was a wise choice. This provides a much cleaner sample for comparisons, although the BPD infants are still not as well described as they might be along some parameters.

However, a number of issues remain and should be raised. At times, it is not at all clear exactly what the predictive intent of the study is. It would appear that the principal investigator is interested in predicting infant growth, but it is less clear whether prediction to infant developmental status is planned. The statement of the problem in the proposal suggests that this is so, but the data analysis section does not describe such a strategy. It seems likely that this is within the principal investigator's plan, but the lack of specificity within the data analysis section made this difficult to confirm. Furthermore, the data analysis section which describes analyses to be conducted relative to each of the three major hypotheses does not always clearly match the hypotheses.

While the domains the principal investigator has chosen to measure are well thought out and important, the choice of some of the measurements remains at issue. For example, in the area of language, the Sequenced Inventory of Communication Development is an extremely limited standard measure, and the notion that language samples of infant vocalizations at 3 months and infant verbalization at 12 months will produce something meaningful is questionable at best. Language skill measurement is difficult at these periods, and more thought about these measurements is suggested. There is also some question as to exactly what the Parenting Stress Index measures. Does it predict or relate in some meaningful way to other stress measures or behaviors likely to be indicative of stress response? And how is maternal depression a "stress" index? It seems more a symptom or mood index. In addition, the Family Environment Scale personal growth dimension typically produces unreliable scores (poor internal consistency), and, including the five scales which comprise that index, may be more problematic than informative.

The sampling plan has changed, in most ways for the better. However, little information is presented concerning the demographic composition of the infants likely to be enrolled in this study. Also, the sample has decreased in size across the three groups to be included. Assuming, as the principal investigator has done, that 60 subjects will remain per group by the 24-month assessment, will all the analyses planned be possible without violating important statistical assumptions? This is an issue particularly for the regression analyses, depending upon how they will be accomplished.

SINGLE PARENTS AND EARLY INTERVENTION PROGRAMS: PARTICIPATION AND GOODNESS OF FIT

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PROJECT NUMBER MCJ-420598

PROJECT PERIOD 10/01/90–09/30/94

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	176,038	153,216	194,027		n/a
Requested	182,044	217,601	227,364	179,592	n/a

* Indirect included

SUMMARY

Statement of the Problem

Urban, low-income, single-parent mothers tend to experience a substantial number of chronic stressors that can constrain their functioning as parents. For those with biologically vulnerable children, early intervention programs (EIPs) have the potential of becoming a significant and supportive resource, an idea that is embraced in P.L. 99-457. Unfortunately, low-income single parents have traditionally been the least likely to become involved in EIP parent-related services. Such a pattern of disengagement with educators and other helping professionals can leave children at risk and their families underserved, despite the availability of excellent child-focused programming.

Currently, there is little data-based information available to guide practitioners in successfully promoting involvement of low-income single parents. In addition, the specific types and patterns of parent involvement in early intervention programs that may foster positive child and family outcomes are not well understood. The results of this study should provide practitioners with data-based guidelines for individually matching services with specific family characteristics and needs, thus enhancing parental participation and improving developmental outcomes

Research Questions or Hypotheses

The theoretical framework guiding the hypotheses asserts that the child is part of a larger, dynamic ecosystem, and thus, child and family outcomes are a function of the interactions within and between the individual child, the child's nuclear and extended family, and the service delivery systems with which they are involved. This project is designed to address four sets of hypotheses involving variables within each of the major domains of a child's and family's ecosystem.

1. The first set of hypotheses addresses the general question of which combinations of parent and family characteristics best predict parent involvement with early intervention programs. It is hypothesized that stress is positively related to parent involvement in EIPs for parents with more effective family functioning and/or greater supportive resources. In addition, stress is predicted to be positively related to involvement in early intervention programs when parents have more internal locus of control and/or perceive the EIP environment more positively.
2. The second set of hypotheses examines relationships between parent and family variables and the child's condition that predict parental involvement in early intervention programs. One hypothesis states that the severity of the child's handicapping condition will be positively related to participation in early intervention programs for parents who show more internal locus of control and/or who have more effective family functioning. Another hypothesis predicts that perceived difficulty with child temperament will be positively related to EIP involvement for parents who have fewer family resources and/or a more positive perception of the EIP environment.
3. The third set of hypotheses links both parent and family variables and service delivery variables with parent involvement in early intervention programs. One hypothesis predicts a positive relationship between parent involvement in early intervention programs and the availability of EIP instrumental support for parents who are more stressed and/or have fewer resources. A second hypothesis predicts that greater parent-focused EIP activities will be related to more EIP involvement for parents who are more stressed and/or have less effective family functioning.
4. The final set of hypotheses links parent and family variables and parent involvement variables with parent outcomes. One hypothesis predicts that greater parental involvement in parent-focused EIP activities will be related to less parenting stress and more parenting satisfaction, particularly for those parents who have fewer supportive family resources. Parent participation in active roles within early intervention programs is expected to be positively related to more appropriate and higher quality parent-child interaction as well as to greater parenting knowledge, particularly for those parents with more ineffective family functioning and fewer social resources.

Study Design and Methods

This is a nonexperimental, hypothesis-guided, exploratory study. The overall thrust of the multivariate design is to assess the significance of service delivery variables in relation to outcome by examining their influence in involving parents in the programs, rather than comparing the relative effects of different models of service delivery. Similarly, the relevance of child and family variables is examined, particularly in relation to how these influence parent participation and how parents benefit from particular program services.

Data are collected in three phases: (1) At the initial entry of the child into the center, data are collected on child variables, parent and family variables, stress, and parent expectations of EIP services; (2) during the 9-month participation period, actual parent participation and parent-related service delivery data are sampled on four different occasions for 2 weeks at a time; and (3) a final assessment is conducted at the end of 9 months to determine parenting outcomes.

Child data are collected by a combination of direct standardized assessment and by completion of standardized questionnaires with the mother. Instruments include the Bayley Scales of Infant Development, the Functional Status Inventory, and the Difficult Child Scale of the Parenting Stress Index.

Parent and family variables are conceptualized according to the level of the parent's relationship system that is being addressed (individual parental subsystem, parent-child dyad, or family/network system). These variables are measured through a combination of direct observation and standardized questionnaires; all questionnaires are completed within an oral, semistructured interview format due to wide variability in parental reading skills in this population. Specific questionnaires related to the individual parental subsystem include the Brief Symptom Inventory, the drug/alcohol portion of the 1989 National Health Survey, the Parent Coping Inventory, the Knowledge of Child Development Scale, and the Child Locus of Control Scales. Stress on the parent/family system is assessed with Abiden's Parent Distress Scale of the Parenting Stress Index and Dunst's Family Needs Scale.

Questionnaires that focus on the parent-child relationship include the Satisfaction with Parenting Scale and the Parent-Child Dysfunction Scale of the Parenting Stress Index. Twenty-minute samples of parent-child free play are rated with the Parent/Caregiver Interaction Scale. Questionnaires that focus on the family/network system include the McMaster Family Assessment Device, the Social Relations Inventory, and portions of Jones' Index of Social Resources.

Questionnaires that focus on the parents' relationships with helping professionals, particularly those within the EIP context, were developed by the principal investigators. The parents' perceptions of the EIP environment are measured with an adaptation of Moos' Group Environment Scale and Community-Oriented Programs Environment Scale. Parents' expectations regarding specific EIP services to be received and the extent to which they expect to be involved with EIP activities are measured with the Inventory of Service Expectations, adapted in part from the Family-Focus Intervention Scale, and with the Professional Relations Inventory, adapted from the Social Relations Inventory.

A behavioral record, the Record of Family-Staff Interactions (RFSI), has been developed by the principal investigators to measure ongoing staff-initiated efforts to engage parents with EIP activities and the rate of actual parent participation. Variables related to staff-initiated efforts include total outreach to the family, the percentage of outreach efforts that are parent-focused, and the availability of instrumental support at the EIP. Variables related to parent participation include the quantity and quality of participation and the percentage of participant activities that are parent-focused or provide opportunities for the parent to have an active role. Data are collected from EIP staff, using the RFSI, at four different times during the course of each parent's 9-month participation in the study.

Population Description and Sampling Plan

The sample consists of 240 families drawn primarily from Philadelphia. Our numbers allow for an attrition rate of 20 percent. Data collected on the more than 1,500 children in Philadelphia EIPs in 1986–87 indicate that 53 percent were African American, 34 percent were white, and 8 percent were Hispanic. Our sample attempts to reflect this racial/ethnic composition. Estimates suggest that low-income, single-parent families represent 45–50 percent of all families served by the Philadelphia EIP system. During the first 3 years of the project, approximately 80 families per year are recruited from the population entering the EIP system for the first time. Parents are paid for their participation in the study.

Families eligible to participate in the study must meet the following criteria: (1) The primary caregiver is single, although she may be currently living with a relative or a male partner; (2) the child is between 6 months and 3.2 years of age; (3) the child was enrolled in either a center-based or home-based EIP within the past 6 months; (4) the child meets the definition of handicapped as outlined in P.L. 99-457, Part H, which may include at-risk children; and (5) the household is low income (i.e., the parent is eligible for food stamps, Aid to Families with Dependent Children, or medical assistance). Families are excluded if the primary caregiver is functionally retarded or actively psychotic. Demographic data are collected on mothers who decline to participate or who drop out, in order to determine whether those who participate differ from these groups.

Analysis Plan

Given the large number of variables in the study, the first task is to reduce the data for a more manageable set of analyses. Techniques utilized include factor analysis of the measures and the creation of composite indices for some variables. The first three sets of hypotheses predict parent participation in the EIPs. Main and interaction effects are tested with multiple regression analyses. The general format is to enter the control variables as a set, followed by the independent variables, and, finally, the cross products of the variables as interacting in relation to the dependent variables. Exploratory analyses are conducted which examine multiple combinations of independent variables to explain participation, such as parents who exhibit high stress, low resources, and poor family functioning. This may involve collapsing ranges into categories and using analysis of variance.

The fourth set of hypotheses predicts parent behavior, knowledge, satisfaction, and stress at the end of 9 months in the program. We examine the effects of parent participation, now treated as an independent variable, together with specific service utilization behaviors by parents in interaction with initial family measures, as they relate to the dependent outcome variables. Regression analyses explore the direct and interactive relations, controlling for initial parenting characteristics and relevant demographic variables. The contribution of parental involvement to the variance in the equation, above the variance explained by the family variables, is also evaluated. We expect adequate variability in the indices of opportunities for parent involvement across the EIP centers.

PRE-AWARD EVALUATION

Originality and Importance

This study would be very useful to program directors and policymakers at national and State levels as they plan and implement early intervention services required by P.L. 99-457. Although the literature on program models and efficacy is slowly growing, there have been very few studies focusing on low-income, single-parent families with a young disabled child. In addition, this study would provide more information on parent participation and involvement, which is necessary for implementation of service systems that are family focused and community based. The new Title V legislation requires that all States develop such systems for children with special health needs.

Regional and National Significance

This study would have regional and national significance, especially since the findings apply to low-income, high-stress, urban single parents. To date, much of the research in this area has been conducted on white middle-class families. Research on this urban population is timely and important

Scientific and Technical Merit

This is a revision of a previously approved but not funded application (which was, in turn, a revision of a previously submitted but not approved application). While the Review Committee was quite positive about the previous proposal, several flaws in the conceptualization and methods were noted and have been addressed in this revision.

In general, this is a well-written, well-organized, and detailed proposal (although the principal investigator is strongly encouraged to observe the guidelines on page limits). The changes between this and the prior submission are clearly stated in an introduction. A thorough understanding of the factors that predict sustained parental involvement in the educational program of children with special health needs is an important and challenging problem, and it is likely that such information will be obtained from the results of this study.

The problem is clearly stated. However, there is some concern about what constitutes early intervention in this proposal, and, thus, what types of children would be studied. The proposal states that children and families will be selected only from early intervention programs funded in accordance with P.L. 99-457. Although this includes children who are at risk for developing a handicap, it is estimated that this group will comprise only a small segment of the sample.

The review of the literature is excellent and reflects a clear understanding of the issues and the literature. The hypotheses are detailed, clearly specified, sophisticated, and reasonable. Questions about the hypotheses raised in the previous round of reviews have been addressed in this revision. The hypotheses now match the data analytic techniques, and it is clearer that study variables are assessed on interval scales. A significant improvement is the reconceptualization of child variables from control variables to independent variables. To incorporate this change, the principal investigator has added an additional set of hypotheses which specify an interaction between parent and child variables predicting participation. The overall conceptualization of the study is theoretically sound.

The section on measures is very thorough and informative. The authors provide good rationales for their choice of measures. There are more age-appropriate measures of children's cognitive level: The Bayley Scales of Infant Development will be used for children under 2½ years of age, and the Stanford-Binet Intelligence Scale (Form L-M) will be used for children between 2½ and 3 years of age. The principal investigator has also provided a clearer justification for the Parent/Caregiver Involvement Scale (PCIS), and discrepancies between PCIS administration directions and the time allotted previously for play observations have been corrected. Reliability for the dependent measures will be established by testing whether child temperament will be adequately assessed by the child domain subscales of the Parenting Stress Index. The reviewers are not familiar with this scale. However, the fact that its concurrent validity has been established with the Achenbach Child Behavior Checklist suggests that it is not an adequate measure of temperament. The principal investigator should consider using a more established measure. In general, the instruments are well described, and evidence of their reliability and validity is provided.

The data analyses are clearly specified and appropriate. It appears that there will be adequate statistical power to do the proposed analyses.

The description of the sampling plan is clear, but the proposal does not specify why data will be collected in three waves (over 3 years), rather than recruiting subjects continuously until the desired sample size has been achieved. No analyses examining cohort effects are described, suggesting that this is not a consideration in the sampling plan. The principal investigator states that each year only the first eligible and willing 80 families will be used in the study, but if more families are available, it would be preferable to recruit them and potentially shorten the length of the study period.

The timeline is reasonable if one accepts the logic of spreading the data collection over 3 years. However, if subjects were recruited continuously, it might be possible to complete the project in 3 years.

This is an ambitious and carefully designed project that should yield data with important public policy and service implications. The recommendation is for approval, but with a reduction in length to 3 years and a reduction in the budget to reflect a smaller contribution of the principal investigator's time.

ADOLESCENT MOTHERING AND PRESCHOOL BEHAVIOR PROBLEMS

GRANTEE	University of Washington
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PROJECT NUMBER	MCJ-530589
PROJECT PERIOD	10/01/89–09/30/92

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	313,132	260,859	203,669	n/a	n/a
Requested	208,898	242,190	219,451	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

This study follows a sample of adolescent mothers and their infants in the preschool years to examine the role of parenting behaviors in the development of behavior problems. Research suggests that serious school-age conduct problems typically have their roots in parent-child interactions during the preschool period, but parent-child interactions at this age have not been studied extensively in populations of adolescent mothers and their children. The study sample is 79 percent white, 10 percent African American, 5 percent Native American, and 6 percent other ethnic backgrounds. Although the study does not specifically address ethnic differences, these could be studied by secondary data analyses. The study will specifically address sex differences in the development of behavior problems.

Research Questions or Hypotheses

This study addresses the following hypotheses:

1. Quality of parenting at each age point will be related to concurrent measures of child compliance, inappropriate behavior, and behavior problems.
2. From Time 1 to Time 2, changes in parenting quality are influenced by the presence of vulnerability or protective mechanisms in the mothers.
3. Severity of behavior problems will be stable from Time 1 to Time 2, except as influenced by changes in parenting quality.
4. Adolescent mothers who have not completed important life transitions to young adulthood will demonstrate more inappropriate parenting than adolescent

mothers who have completed this transition successfully; similarly, the children of mothers who have not completed these transitions will demonstrate more behavior problems than the children whose mothers have done so;

5. Children with stable attachments from infancy through Time 1 will have fewer behavior problems at Time 2, compared to children with insecure attachments from infancy.
6. Boys will evidence more externalizing behavior problems (including conduct problems) than girls. Boys who have insecure attachments in infancy followed by poor parenting or additional vulnerability factors during the preschool years will be more vulnerable than girls to developing conduct problems.

Study Design and Methods

This project is a modified sequential longitudinal study which is quasiexperimental in nature. The study population consists of two cohorts of preschoolers drawn from a sample of 209 children who participated in an earlier study of adolescent parenting and infant attachment at 1 year of age. These cohorts are followed concurrently across a 1-year period and are assessed at two preschool ages on the outcome variables of behavior problems, compliance, and inappropriate behavior. Cohort 1 is assessed at ages 3½ (Time 1) and 4½ (Time 2), and Cohort 2 is assessed at ages 4½ (Time 1) and 5½ (Time 2). The major independent and dependent variables are assessed at both Time 1 and Time 2, permitting comparisons of development processes at three different ages across the preschool period. The six sets of independent variables include measures of infant security of attachment, parenting, maternal vulnerability, maternal protective mechanisms, child vulnerability mechanisms, and child protective mechanisms. Additional analyses are made on the longitudinal data from Time 1 to Time 2 for each cohort and for the combined sample in order to examine influences on developmental pathways. Thus, some of the study's hypotheses reflect cross-sectional issues, and some reflect longitudinal issues.

The home visit begins with the interviewer explaining the study's purpose and procedures to the mother. The interviewer then administers five interview instruments: Interview and Demographics; Child Vignettes; Mother's Social Network, Part I and Part II; Child's Social Network Interview; and Difficult Life Circumstances. The interviewer requests that mothers whose children are in child care, nursery school, or kindergarten settings at least half-time sign a letter of consent authorizing the provider to complete the Preschool Behavior Questionnaire, which is then mailed to the provider. The home visit concludes with the interviewer paying the mother $20 and obtaining the names of three people who could help locate the mother if she relocates before completing the study. The interviewer completes the Home Observation for Measurement of the Environment and the Adult Conversation Skills Scale after leaving the subject's home.

The laboratory visit is scheduled to occur within a week following the home visit. The Test for Auditory Comprehension-Revised is administered to the child, while, in a different room, the mother completes the Parent Opinion Questionnaire. Then, the mother is brought into the playroom for the first of two videotaped sessions involving mother-child interactions: the child's game/parent's game/clean-up. During this session, the mother wears a "bug-in-the-ear" radio receiver to allow the experimenter to communicate unobtrusively from the adjoining observation room.

At the conclusion of the child's game/parent's game/clean-up assessment, the mother and child have a break and a snack, and then the mother is taken to an interview room where she completes a questionnaire packet containing the Life Experiences Survey, Child Behavior Checklist (CBCL), Beck Depression Inventory, Parenting Sense of Competence Scale, O'Leary Porter Scale, and the Parent Aptitudes Tests. Mothers of 5½-year-old children also complete the Disruptive Behavior Disorders section of the revised Parent Form of the Diagnostic Interview for Children and Adolescents.

While the mother is answering the questionnaires, other tests are being administered to the child. The Pictorial Scale of Perceived Competence and Social Acceptance for Young Children is administered to 4½-year-old children. The Separation Anxiety Test is administered to both 4½- and 5½-year-old children. Only the 5½-year-old children are asked to draw their family and complete three subscales of the Peabody Individual Achievement Test-Revised. The mother returns to the playroom after completing the questionnaires. The reunion is videotaped and later coded for attachment security, using the method of Cassidy, Marvin, et al. The mother receives $20 for the laboratory visit and $20 for the questionnaire packet. If she has completed Time 1 and Time 2 assessments, she receives an additional $60.

Population Description and Sampling Plan

The sample was originally recruited in a 1986–1989 study on psychosocial and environmental factors related to infant attachment security (Mothering in Adolescence: Factors Related to Infant Security, MCJ-530535, Susan J. Spieker, Principal Investigator). The original sample consisted of adolescent women who are primarily white (79 percent), unmarried (80 percent), with at least a high school education (61 percent). The average age of the mothers in the original sample was 17.1 years at time of delivery; 43 percent of the children born to these mothers are male.

Of the original study sample, 57 percent ($N = 120$) were recruited into the followup study. Attrition over the course of the project is estimated to be 10 percent. Subjects were originally recruited from clinics, schools, and adolescent parent programs in the greater Seattle area. Subjects were included if the target child was born before the mother's 20th birthday, and if the mother chose to parent her child.

Analysis Plan

The hypotheses of this study are a limited subset of those we are likely to test. The study will yield a rich and complex data set. We are guided by both attachment and social learning theories to generate additional hypotheses and research questions. The method of analyzing the data associated with each of the stated hypotheses is described below. Prior to multivariate analyses, univariate and bivariate analyses are performed. The distribution of each variable is examined to identify outliers and determine whether transformations of the data should be performed to create more appropriate distributions for the multivariate analyses.

The analyses are somewhat complex because: (1) More than one dependent variable is involved; and (2) the independent variables are collected on two occasions for each cohort. Furthermore, cohorts 1 and 2 are combined for some analyses: All subjects are included in the age 4½ analyses, and all subjects are included in analyses for which time is a factor. We need to know about group differences at each time point as well as changes over time for each measure. The general plan is to perform the major multivariate analyses at each time point to assess attachment group differences on the behavior problem outcomes. A series of univariate analyses is performed (infancy attachment × time) to assess changes over time in all of the independent and dependent variables. The demographic characteristics of the mothers and children in cohort 1 and 2 are examined, using multiple *t* tests, with Bonferroni corrections, to ensure that the two cohorts do not differ significantly. Group differences and age differences on measures that yield nominal-scale results, such as the Ainsworth Strange Situation, are analyzed nonparametrically. For example, a chi-square analysis is performed to determine whether there is a systematic relationship between infancy attachment classification at Time 1 and Time 2. Age changes in classification within the original infancy attachment groups are analyzed by means of McNemar's test for the significance of changes.

Two cohorts are combined for the data analyses on 4½-year-old children and for the major multivariate analyses in which time of measurement (Time 1 and Time 2) is a factor. For these analyses, T-scores from the CBCL and percentages of child compliance and inappropriate behavior are used to enable data from 3½- and 4½-year-old children (Time 1) and 4½- and 5½-year-old children (Time 2) to be combined. T-scores on the CBCL are also used in order to combine analyses for both boys and girls, since different raw scores designate risk and different narrow band syndromes apply for boys and girls.

The univariate and multivariate analyses are based on dichotomizing the independent variables so they can be used as factors (e.g., infancy attachment × parenting × maternal vulnerability mechanisms × maternal protective mechanisms) in multivariate analyses of variance (MANOVA) and analyses of variance (ANOVA). Dichotomizing the independent variables are determined by an examination of the data and/or a priori decisions based on previous research. Alternatively, since it is important to utilize the richness of these data, the measures within each independent variable may be aggregated, creating summary indices or adding standardized scores. The aggregated score could be entered into a hierarchical multiple regression in which specific interactions are tested (e.g., infancy attachment × parenting) using effect coding. The actual method is governed by the nature of the data set and the relevant hypothesis. In general, we feel that robust findings will be revealed by either approach.

PRE-AWARD EVALUATION

Originality and Importance

This study of the development of behavioral problems in a high-risk population targets the preschool age because of its importance to the initiation of problem behaviors and the potential for early intervention. This project could make an important contribution to understanding the role that various vulnerability and protective mechanisms have.

Regional and National Significance

The population under study is a semirural, mostly white, population of adolescent mothers. Since the majority of adolescent mothers in this country are white, it is important to know parent-child interaction patterns and development for intervention purposes. The majority of the population has a history of physical and sexual abuse, half the mothers are depressed, and the mothers are likely to encounter severe difficulties in raising their children.

Scientific and Technical Merit

This well-documented and well-written proposal presents a model of development which it will test by collecting data on a sample of adolescent mother-child dyads. There are two issues with this proposal that should be addressed. First, there is little mention in the proposal about substitute care (family care, nursery school) that the infants and children may have had. It is possible that these institutions would have important socialization consequences for the child.

The second issue is a conceptual one. This study builds upon the attachment model. However, there are now a number of well-delineated critiques of both the outcome studies and the empirical bases for accepting the Ainsworth Strange Situation Procedure as a valid index of attachment and of the attachment classifications as predicting outcome. The study also accepts the addition of a fourth classification, "D" (for disorganized), although there are few data on this classification other than from the developer of this classification. In addition, the study would assess attachment after 1 year of age, using a system developed by the MacArthur Network working group that has little reliability and no validity data to back it up. There are debates in the literature about these issues, and they are not resolved. The current proposal does not acknowledge these debates.

The analytical plan in general is appropriate to answer the research questions. In addition to the analyses which are planned, it would be very useful to look at the magnitude of some interaction terms. For example, Specific Aim 6, which examines gender differences, will be approached using separate analyses by gender. One should also look at interaction terms involving gender as a means of comparing the two analyses. Because the CBCL defines behavior problems differently for males and females, it may not be straightforward to compare the gender differences using the gender differences using the gender-specific scales.

There are other special analytic problems which arise in examination of the vulnerability and protective mechanisms. The analytical plan calls for inclusion of dichotomous variables for vulnerable and protective characteristics, but it may be more reasonable to create a trichotomy and test differences between those with vulnerable factors, those with protective factors, and those with neither.

In general, the analyses which plan to combine the two cohorts are appropriate. In the growth curve models which use time as a factor, it would be important to examine the correlation structure of the measures since changes in correlation across time may require multivariate growth curve modeling rather than the univariate modeling described in the proposal.

DROWNING PREVENTION THROUGH SWIMMING LESSONS

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PROJECT NUMBER MCJ-530607

PROJECT PERIOD 7/1/91–6/30/93

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	220,188	227,758	n/a	n/a	n/a
Requested	224,126	227,758	n/a	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

Drowning is the third leading cause of death in children ages 0–4 years. Several measures designed to prevent these drownings have received considerable attention; of these, the teaching of swimming and water safety to young children has been most vigorously promoted. Although such programs have been implemented by the Red Cross, the YMCA, and private organizations, and have been widely publicized by the mass media, their effectiveness in reducing mortality and morbidity has never been evaluated empirically.

The purpose of this study is to determine whether preschool children trained in swimming and water safety are less likely to drown than those who have not been trained. This study has major implications for the development of drowning prevention programs for children in this country. If the training proves effective, resources of various organizations can be directed to intensively promote training in swimming and water safety within this age group. However, if the training program is found to be ineffective, other methods of prevention need to be examined.

Research Questions and Hypothesis

This study tests the following hypotheses: (1) Children with water safety training will exhibit safer behavior at poolside than children without such training; (2) children with training will act more competently in a simulated drowning situation than children without such training; (3) parents of children with water safety training will have a clearer understanding of the child's abilities and limitations than parents of children without such training; (4) children's water safety behavior will correlate positively with

their swimming ability; and (5) the developmental level, temperament, and personality of the children will have an independent effect on water safety behavior prior to training, and on subsequent changes due to instruction.

Study Design and Methods

This research uses a clinical control trial design with repeated measures at four points in time. The study recruits 130 preschool children between 24 and 42 months of age, and assigns them to either 8 weeks (delayed intervention) or to 12 weeks (immediate intervention) of biweekly swim lessons. These lessons, designed for preschoolers, are based on the nationally recognized Red Cross and YMCA swim programs. The lessons emphasize two sets of skills: (1) Out-of-water safety behavior (safe deck behavior), and (2) swimming skills. Swim instruction is conducted in groups of approximately six children, accompanied by their parents. Instructors are trained by the Children's Hospital and Medical Center swimming program director, who conducts random quality control checks throughout the study.

Children's water safety skills and ability to swim to safety are measured by initial observation in both the delayed and immediate intervention groups (time T1). The second observation is conducted after 8 weeks of training for the immediate intervention group, and after 8 weeks of no training for the delayed intervention group (T2). The third observation is conducted after an additional 4 weeks of training for the immediate intervention group, and after 8 weeks of training for the delayed intervention group (T3). The final observation is conducted after 12 weeks with no additional training in each group (T4).

A number of child and family variables are assessed. Children's water safety skills, including risk of falling in (deck behavior) and ability to swim to safety, are measured at T1, T2, T3, and T4. Children's swimming skills are measured at the beginning and end of each child's water safety course (T1 and T3 for the immediate intervention group and T2 and T3 for the delayed intervention group). Prior to the first observation and last observation, parents are asked to estimate their own abilities and comfort level in water as well as their perception of their children's skills and comfort in the water.

At the start of the study, information is collected on family demographics (Hollingshead Two Factor Index of Social Position), the children's developmental level (Minnesota Child Development Inventory), and their behavior (Child Behavior Checklist).

Population Description and Sampling Plan

Children are recruited from middle-income Seattle—King County child care centers located near the public pools used in the study. The study includes only those children who have had no prior swimming training and excludes children who have a chronic medical or developmental disability. To ascertain eligibility, parents are required to fill out the revised Denver Prescreening Developmental Questionnaire. Children are 24–42 months of age at the time of entry into the study, so that the intervention can be completed before the children reach 4 years of age. The children are divided into the two groups (immediate intervention and delayed intervention), with 65 children per group.

There will be a total of 130 children in the study. Based on current experience at the Children's Hospital and Medical Center swim program, it is estimated that 20 percent of children ages 2–3 years will have correct deck behavior before water safety training, and the same number will have the ability to pass the recovery test. Two comparisons are used in the sample size estimates: Skills before training will be compared to skills after training, and children's skills after training in the delayed intervention group will be compared to those in the immediate intervention group. We estimate that 40 percent of children in the immediate intervention group will have correct deck behavior, and that a similar percentage will pass the recovery test after training. This gives a response difference of 0.20, compared to pretraining. The number of total subjects needed in the study, using a one-sided alpha of 0.05 (since we expect that the children's performance will improve) and a power of 0.8, will be 130. This sample size will allow us to detect a difference of .20 between the skills after training in the delayed intervention group, compared to the immediate intervention group. We will recruit a total of 150 subjects, to allow for dropouts.

Analysis Plan

The data analysis has three broad goals: (1) Test the hypotheses stated above; (2) quantify the effects of water safety training on water safety behavior; and (3) determine parent and child characteristics that influence acquisition of water safety skills and swimming ability.

The chief outcome variables are water safety skills and swimming ability, as measured by several instruments. The responses to each instrument are combined to form a fairly continuous score. Single items are also analyzed to determine frequency of specific safe behaviors in relation to the intervention.

Exploratory analysis is initially carried out using histograms, frequencies, scatterplots, boxplots, and cross-tabulations. The exploratory analysis identifies variables that need transformations (such as log) for further analyses, or that should be analyzed by nonparametric methods.

Effects of the intervention are determined by comparing water safety skills (such as deck behavior) after training in the immediate intervention group to water safety skills in the delayed intervention group. The simplest analyses are paired *t* tests and t-based confidence intervals for the differences in performance. The Wilcoxon signed-rank test is used for highly non-normal distributions.

The joint effects of multiple factors on safety behavior are analyzed, using least-squares regression. The dependent variable is performance (e.g., deck behavior), measured postintervention in the immediate group and preintervention in the delayed group. Independent variables include a dummy variable identifying group membership, initial performance level, and other predictors of skill acquisition, both alone and included in interaction terms with group membership. Standard hypothesis tests for nonzero regression coefficients are used. The magnitude of the coefficients indicates the size of the effects of independent variables on safety behavior.

Another set of analyses is concerned with the time pattern of acquired skills:

1. Postintervention—Preintervention = Maximum gain in skills;

2. Followup—Preintervention = Net gain in skills; and
3. Followup—Postintervention = Retention of acquired skills.

These changes are examined by paired *t* tests (with each child as a self-matched control) and t-based confidence intervals. Regression is used to determine the effects of covariates on the change variables described above.

Multivariate analyses of variance and covariance are used to determine whether there are differences in the ensemble of outcome measurements (and their changes) between the immediate and delayed training groups.

PRE-AWARD EVALUATION

Originality and Importance

This study is intended to reduce the numbers of small children who drown each year by falling into water. This is unquestionably an important area of concern, considering that drowning is the third leading cause of death for the target group in this study (children ages 0–4 years).

This project is original in its attempt to apply proxy measures of injury risk in the area of drowning prevention. However, the researcher has used proxy measures in researching other prevention projects, such as bicyclist and pedestrian street crossings.

Regional and National Significance

The study is to be conducted at the Seattle Parks Department pools and the Children's Hospital and Medical Center, also in Seattle. The problem of drowning is not limited to Seattle, and, as noted by the principal investigator, toddler drownings are more frequent in other States.

Although the problem of toddler drowning is not limited in its geographical significance, the anticipated findings would appear to have considerable limitations. Clearly, they are most germane to upper- and middle-income families, who are most likely to have swimming pools.

Moreover, even if the preventive techniques employed in the study are found to be successful, it is unlikely that low-income parents would ever receive such training, due to lack of time, money, or access to the necessary recreational resources. In short, the findings from such a study are likely to have a very limited significance, except for populations similar to those employed in the study.

Scientific and Technical Merit

This extremely well-written proposal has addressed all of the major design, sample, and measurement concerns as well as other concerns necessary to conduct a random control trial. The literature review and rationale for this study are carefully presented and articulated in light of a broad range of injury prevention strategies. The implications of the findings are explained in terms of their national significance for reaching the *Healthy People 2000* objectives in this area. Although other strategies (such as requiring fences around pools) may also be effective, the proposal advocates appropriately for strategies to effect change in individual behavior as well.

The conceptual framework for the study and the basic design utilizing two intervention training sessions (one lasting for 8 weeks, the other for 12 weeks) are thoroughly explained and reasonable. The description of the measures is clear and well defended, for the most part; the description of the swimming measures needs to have more evidence with respect to their reliability and validity. The rationale for using the Hollingshead socioeconomic status measure is not convincing: Why not use income and parental education and occupation separately, especially since there are likely to be many single-parent families in the sample?

Descriptions of the sample, the treatments, the design, and the analysis of the variables collected are well done and reasonable. In sum, this is a well-written proposal which lays out a good research design to assess a program focused on preventing drownings in young children.

Minority Report

The use of parental reports for assessing developmental level is not appropriate. The recommendation is to perform appropriate developmental assessments (e.g., Bayley Scales of Infant Development, McCarthy Scales of Children's Abilities) or not to assess developmental level at all. It is unclear how the effects of mediating variables will be assessed. Specifically, there is a concern that the sample size will not allow enough power or a suitable subject-to-variable ratio to include so many predictors and covariates.

CONTINUATION

GRANTS

HEALTH AND NUTRITION OF U.S. HISPANIC CHILDREN

GRANTEE Stanford University School of Medicine

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PROJECT NUMBER MCJ-060518

PROJECT PERIOD 04/01/88–03/31/91

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	315,670	261,485	271,553	n/a	n/a
Requested	374,447	311,744	346,730	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

This study analyzes data from two National Health and Nutrition Examination Surveys (NHANES I, 1971–74 and NHANES II, 1976–80) and the Hispanic Health and Nutrition Examination Survey (HHANES, 1982–84), in order to identify and quantify the major health and nutritional problems of Hispanic children and adolescents in the United States. It is an extension of an earlier investigation that focused on data for Mexican Americans only. The current investigation, which targets mainland Puerto Ricans and Cuban Americans as well, seeks to:

1. Assess the level of severity of health and nutrition problems for these population groups;
2. Identify factors related to poor health and nutrition;
3. Assess the functional implications of identified health problems; and
4. Identify the major constraints to the use of health and nutrition services.

Data from mainland Puerto Rico are analyzed with the collaboration of investigators from the University of Puerto Rico. This allows more insightful analyses as well as the opportunity to compare the HHANES information to data available in Puerto Rico.

Research Questions or Hypotheses

A series of general and specific hypotheses guide analyses within and between ethnic groups. These hypotheses are organized according to topic areas (i.e., growth and development, nutrition, health status, and health care utilization). Examples of these hypotheses follow:

1. Major differences exist in the nutritional status of the three principal populations of Hispanic children in the United States, as reflected by biochemical, dietary, and anthropometric data;
2. Differences in linear growth between preadolescent children of Hispanic and non-Hispanic origins are not entirely explained by differences in socioeconomic status;
3. The nutritional status of mainland Puerto Rican children is impaired in comparison to Mexican-American, Cuban-American, and non-Hispanic children; and
4. The increased fatness of Hispanic children in the United States is largely in trunk and fat folds. This tendency is more marked in Mexican Americans than in Cuban Americans or mainland Puerto Ricans.

Study Design and Methods

The overall study design is descriptive and correlational. It involves secondary data analysis using univariate and multivariate statistical techniques. A three-tiered approach to the HHANES data is planned. First, we quantify the extent and nature of health and nutrition problems in the Cuban-American and Puerto Rican populations and compare these results to what has already been learned from the Mexican-American component of the survey and from data on non-Hispanic whites and blacks derived from NHANES I and II. Second, we identify variables associated with these conditions to assess whether the pattern of relationships among these exploratory variables differs by ethnic group. Among the variables considered are familial factors such as income, education, household structure, and maternal characteristics; and individual factors such as age, sex, and level of acculturation. Third, we assess the functional implications of abnormal health and nutritional status for Puerto Rican and Cuban-American children, and compare these results with those obtained from Mexican-American children as well as comparative samples of non-Hispanic white and black children derived from NHANES II. In addition, we study utilization of health and nutrition services to evaluate the impact of the nutritional and health status of the three Hispanic subgroups.

Population Description and Sampling Plan

NHANES I and NHANES II are complex national probability surveys of the noninstitutionalized population in the United States. They contain data on approximately 6,700 non-Hispanic children (ages 1–19 years), who serve as a comparison group for our study.

The HHANES was the first large-scale health and nutrition survey to target Mexican Americans, mainland Puerto Ricans, and Cuban Americans, and the sample was obtained through a complex, multistage, stratified, clustered sampling of defined Hispanic populations. Mexican Americans were sampled from the five southwestern States (Arizona, California, Colorado, New Mexico, and Texas); mainland Puerto Ricans were sampled from the New York City area; and Cuban Americans were sampled from Dade County, Florida. This regional sampling technique accounted for 73 percent of all

Mexican Americans, 53 percent of mainland Puerto Ricans, and 55 percent of Cuban Americans who were living in the United States.

The study population consisted of 3,622 Mexican-American children, 1,289 mainland Puerto Rican children, and 378 Cuban-American children, ages 6 months to 18 years. These children represent approximately 3.6 million Mexican-American, 487,000 mainland Puerto Rican, and 113,000 Cuban-American children from the sampled regions. Health status data was collected on all these children via questionnaires, physical exams by survey physicians, selected biochemical tests, and screening examinations. Most of these tests and examinations are similar to those performed previously in the NHANES I and II.

Analysis Plan

The plan for data analysis demands attention to some complex statistical and computational issues. These require an understanding of the complex stratified multistage probability sampling methods used in HHANES. Traditional methods of point and variance estimation and hypothesis testing cannot be used to analyze the data. Special statistical software designed to incorporate the complex sample design into variance estimation is needed to compute sampling variances. Codes are included in the HHANES data base, which allow the analysis to be done using special software recommended by the National Center for Health Statistics. There is instability in some estimates, however, especially for subgroup analyses. The routine analysis proceeds in three steps: (1) Data cleaning and code book development, (2) descriptive analyses, and (3) hypothesis testing.

MATERNAL PESTICIDE EXPOSURE AND PREGNANCY OUTCOME

GRANTEE	San Diego State University				
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PROJECT NUMBER	MCJ-060546				
PROJECT PERIOD	11/01/86–10/31/89				
COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	156,004	168,452	186,313	n/a	n/a
Requested	185,589	195,996	207,645	n/a	n/a
* Indirect included					

SUMMARY

Statement of the Problem

Knowledge of the toxic effects of specific environmental agents and their link to mechanisms of human reproduction is in its infancy. Although evidence indicates that pesticides can pass through the human placental barrier, further study is needed to document unspecified effects and to replicate the results found by current researchers. Spontaneous abortion, low birthweight, congenital anomalies, cleft lip and cleft palate, limb defects, and infertility have been the focus of some recent investigations. Many of those studies found that chemicals in the environment can contribute to the incidence of birth defects and other reproductive harm in the general population. The role of pesticides, in particular, may be significant. Few studies have focused on community exposures to pesticides, which tend to be lower than occupational exposures. Also, few population-based studies have attempted to determine the actual degree of exposure in individual cases.

This study investigates the reproductive effects of organophosphate and carbamate insecticides. Organophosphate pesticides are versatile, widely used pesticides which have replaced organochlorines in popularity since the 1970s. Their mechanism of toxic action is the inhibition of cholinesterase (ChE). Carbamate pesticides are similar to organophosphates in the action of inhibiting cholinesterase, but are generally less toxic because they have a shorter life. This study includes an examination of environmental and occupational exposures, and makes an assessment of degree of exposure through use of repeated measures.

143

In this study, the protocol for ascertaining pesticide exposure is incorporated into routine prenatal care. The value of this approach is that it demonstrates the feasibility of monitoring pesticide exposure routinely in pregnancy when environmental or occupational risk is suspected. Additionally, in areas where there is a high volume of pesticide use per acre, a standard protocol for collection of blood samples to test for cholinesterase (to use as a baseline value) could be recommended to providers who care for women preconceptionally (e.g., at family planning clinics). In addition to having immediate utility, such data will be available for retrospective analysis of outcomes occurring over the years of growth and development of the offspring born to these women. For women who are already pregnant, the collection of biologic samples for cholinesterase baseline values could be implemented at the postpartum visit.

Research Questions or Hypotheses

The study tests the following hypotheses:

1. There is no difference in the blood cholinesterase activity between women who report exposure to pesticides during pregnancy and women who report no exposure;
2. There is no difference in the occurrence of spontaneous abortion between women who have been exposed to cholinesterase-inhibiting pesticides and those who have not been exposed;
3. There is no difference in the occurrence of preterm labor between women who have been exposed to cholinesterase-inhibiting pesticides and those who have not;
4. There is no difference in the occurrence of low birthweight infants between women who have been exposed to cholinesterase-inhibiting pesticides and those who have not; and
5. There is no difference in the occurrence of toxemia of pregnancy between women who have been exposed to cholinesterase-inhibiting pesticides and those who have not.

The related objectives of the study are to:

1. Identify physiologic versus pathologic levels of cholinesterase throughout pregnancy;
2. Use biologic monitoring of pesticide exposure to verify self-reported exposure;
3. Identify the study variables most highly associated with cholinesterase levels;
4. Determine the most appropriate comparison group; and
5. Ascertain levels of cholinesterase in fetal cord blood.

Study Design and Methods

A prospective cohort design is used. The study follows a cohort of 535 women throughout their pregnancies, through interviews on history of exposure, collection of biologic specimens, and review of maternal and newborn records. Biologic specimens are used to verify the pesticide exposure experience (exposed versus nonexposed) of the cohort members as reported in interviews. Data from maternal and newborn patient records are used to verify previous health and reproductive history and to determine current pregnancy outcome. Comparisons of the pregnancy cholinesterase activity and of selected pregnancy outcomes are made between the two exposure groups.

Three assessment measures are used: A questionnaire (consisting of three modules) to determine self-reported exposure history and potential confounding variables; maternal patient records (primarily the Hollister Prenatal Record System) and newborn patient records; and biologic assay of blood samples for cholinesterase activity in red cells and plasma. Some fetal cord blood assays are also carried out.

The questionnaire items address residential/environmental exposures, the occupational history of the participant and spouse, specifics of potential exposures, pesticide handling and use, and prescription and nonprescription drug, alcohol, and smoking history. The questionnaire was pretested in Spanish and English in order to determine whether it met expectations for participant comprehension and whether the interviewers would understand how to ask questions and record the responses accurately.

There are eight data modules in the complete data set, three of which are included in the questionnaire (the master data form, initial interview and assessment, and ongoing exposure assessment). The other five modules (health history summary, reproductive history, nutritional assessment, birth outcome, and laboratory) are completed primarily by patient record review.

The Hollister Prenatal Record System is used for the study subjects. This system is designed to identify women at risk for a problem pregnancy, based on their current medical condition and their socioeconomic history. It is widely used and is a standard, accepted system among prenatal and perinatal obstetric practitioners. Newborn and birth outcome information is abstracted from hospital records at the facility where delivery occurred.

The final measure used for the study is biologic assay of blood samples for cholinesterase activity in red blood cells and plasma of participants and their neonates. The main objective of biologic monitoring is to obtain laboratory results to use in classifying participants for evidence of exposure to pesticides during pregnancy. A secondary objective is to investigate normal blood cholinesterase fluctuations in pregnancy. For purposes of validation of this measure, two comparison groups are designated. Comparison group 1 consists of 25 pregnant women who are not employed in an occupation normally associated with pesticide use, and who live outside the study area. This group is the control for exposure. Comparison group 2 consists of 25 nonpregnant women living in the study area who are controls for pregnancy.

Population Description and Sampling Plan

The study population is comprised of women enrolled in the North County Health Services (NCHS) Perinatal Program. All attend NCHS clinics in northeastern San Diego County. They are primarily Hispanic women of low income and low educational status, and many have recently emigrated from Mexico. The average age is in the mid-twenties, and the majority have more than one child. Because agricultural production in northern and eastern San Diego County is among the highest in the State, these women are considered to be potentially exposed, occupationally and/or environmentally.

The NCHS Perinatal Program serves approximately 300 pregnant women each year. The study was described verbally and in writing (in the women's native language) to all patients entering the perinatal program between January 1987 and December 1989. They were then asked to participate. Those who agreed to participate signed informed consent forms. Approximately 75 percent of the women entering the clinic during this period participated in the study. There is no difference in the sociodemographic and reproductive characteristics between those who agreed to participate and those who did not.

Analysis Plan

Statistical techniques employed were standard descriptive measures, chi-square and the Mantel-Haenszel extension of chi-square, partial correlation, analysis of variance, and relative risk. Confounding variables, particularly the effect of pregnancy, drug/alcohol/smoking habits, and other environmental factors, are controlled in the analysis where appropriate and where cell size is sufficient.

The self-reported exposure questions from the survey instrument are dichotomous, yes/no questions. In order to determine their relationship to cholinesterase levels, analysis of variance of group cholinesterase means is employed. First, all exposure questions are grouped as indicative of environmental and agricultural exposure, household exposure, or none/limited exposure. These grouped exposure questions are then reevaluated to identify attendant conditions that would represent chronic or long-term exposure. This is done because of the relatively short time that the pesticide stays in the system (affecting the ChE level) and the random collection of blood samples; acute, high levels of exposure cannot usually be captured with periodic scheduled blood sampling unless the scheduled phlebotomy happened to occur within 1 or 2 days of exposure. After several combinations (groups) of exposure questions are created, the analysis of variance of cholinesterase means by groups is used to select the group in which the questions and the plasma levels are most highly correlated.

Level of exposure is calculated by comparison of individual cholinesterase levels with the total study group norm for cholinesterase. Subjects are placed in the high, medium, or low tercile. Finally, the relationship between exposure and the outcome variable is determined by chi-square and relative risk analysis.

Analysis is carried out in five sections: (1) Demographics and health history of the study group; (2) description of plasma cholinesterase levels of the study group–patterns and trends throughout pregnancy and degree of correlation with high or low levels of exposure (hypothesis 1); (3) exposure score development and classification of subjects based on self-reported exposure and plasma cholinesterase levels; (4) determination of the association between pesticide exposure and spontaneous abortion, preterm birth, low birthweight, and toxemia (hypotheses 2, 3, 4, and 5); and (5) description of fetal cord blood cholinesterase levels.

SURVEY OF CHRONICALLY ILL CHILDREN'S USE OF TIME OUT OF SCHOOL

GRANTEE University of California at San Francisco

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PROJECT NUMBER MCJ-060550

PROJECT PERIOD 04/01/87–03/31/90

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	92,138	93,289	91,751	n/a	n/a
Requested	102,085	106,604	104,700	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

The primary aim of this study is to describe and analyze the everyday out-of-school life experiences of chronically ill school-age children and to examine the effects of different ecological contexts on the child's out-of-school life. To accomplish this aim, we focus on the ways in which chronically ill children use their out-of-school time. The use of time is a proxy—an indicator of what matters to children and to their parents. Out of school, the forces of family and neighborhood sort children and send them off in fundamentally different directions; thus, evidence can be obtained about the circumstances in which chronically ill children are raised.

This study includes 400 children and their parents from contrasting ecological contexts, such as different work situations, different family structures, different types of neighborhoods, and different States (i.e., California and Alabama). This approach allows us to examine the effects of those contexts on the patterns of children's use of time. This information will enable us to identify aspects of the experience of childhood life that will affect the quality of later adult life, and the ways that family and neighborhood life are related to the everyday behavior of children. In addition, studying children and their families from a number of ecological contexts gives us greater potential to understand relations that hold across groups, and to make more general inferences regarding these relationships.

Research Questions or Hypotheses

This study addresses the following research questions:

1. What kinds of things do chronically ill children do when they are not in school?

2. What are the effects of family life, family structure, and socioeconomic status on these children's lives outside of school?
3. What are the range of opportunities and constraints that shape children's use of time and their attitudes toward time use outside of school?
4. What roles do neighborhoods have in the out-of-school activities of chronically ill children?
5. What is the capacity of urban environments to serve as support systems to parents directly involved in planning and managing chronically ill children's use of time out of school?

Based on analysis of the pilot data, two general hypotheses have been developed: (1) The pattern of chronically ill children's time use outside of the home depends on the extent and the manner in which parents and others engage the child in joint activities; and (2) the capacity of the parents to engage in such joint behavior depends on the extent to which external support systems exist to provide parents with opportunity, assistance, and resources.

Study Design and Methods

A cross-sectional survey design is used to collect data at one point in time from a sample of chronically ill children and their parents. Data are collected in this survey study by structured interviews in the children's homes. All interviewers receive extensive training and are supervised by the Survey Research Center at the University of California at Berkeley. Interviewers are female, between the ages of 25 and 40, and have an expressed liking for children and a pleasant appearance.

Data are collected for this survey using three time use instruments: The Child Interview Schedule and the Parent Questionnaire, designed by Medrich; and the Medical Treatment Questionnaire, designed by the investigators.

The Child Interview Schedule consists of 59 multiple choice items that evaluate time use in five time domains: The child's independent activities; the child's activities with the parents; chores, jobs, responsibilities, and spending patterns; organized activities; and television viewing. Alterations were made in Medrich's original instruments to acknowledge chronically ill children's use of medical equipment and immobility issues.

The stability of children's responses over time are examined using a three-wave panel design. In the panel study, the same respondents are interviewed with the same questions at different time periods. The first administration of the interview takes place in the child's home. Subsequent interviews at 2, 4, and 6 months are conducted by telephone, and the children are asked a subset of 20 questions from the original interview. Fifty children from each State participate in the panel study. Little information is currently available on the stability of children's response in survey studies.

The Parent Questionnaire consists of 83 multiple choice items which evaluate the parents' values, attitudes, and opinions in six areas: The neighborhood, the child at school and home, the child's activities with family and friends, organized after-school activities, childrearing, and parents' activities. No alterations were made in this instrument.

The Medical Treatment Questionnaire consists of 17 items designed to elicit information from the parent about the child's illness. This instrument asks questions about the child's medical history, parent's perception of illness severity, medical treatment responsibility, medical treatment time, and identification of discrimination which has influenced activity patterns.

Interviewers also collect background data. The Interview Observation instrument collects information regarding the atmosphere during the interview, ethnic background of the family, and a description of the neighborhood.

Population Description and Sampling Plan

The study sample is drawn from the population of chronically ill school-age children residing in the San Francisco and Birmingham Standard Metropolitan Statistical areas. A noncategorical approach focusing on disease commonalities is used; thus, children with a variety of chronic illness types are selected.

The aims of the study, the review of the literature, and the results of the pilot study also indicated some general population specifications: Children in the study (1) are diagnosed as having an organic chronic illness for at least 2 years, (2) are 10–12 years of age, (3) are attending school, and (4) have not moved or changed elementary schools within the past 12 months. Children who are blind, deaf, mentally retarded, or have cancer are not eligible for this study, nor are families who have another child with one of these problems. The survey is conducted in two States: California (the San Francisco Standard Metropolitan Statistical Area, which includes Alameda, Contra Costa, Marin, San Francisco, and San Mateo Counties) and Alabama (the Birmingham Standard Metropolitan Statistical Area, which includes Bibb, Jefferson, Shelby, St. Clair, and Walker Counties). Two hundred children are selected from each of the two States for a combined total of 400.

The sample is drawn from a sampling frame. To locate the sampling frame of a rare population, guidelines by Kish are applied (using the approaches of large clusters and controlled selection). A stratified random sample based on socioeconomic status is drawn from the sampling frame from each State. The random sample for each State then consists proportionately of children from each socioeconomic stratum (high, middle, and low).

Analysis Plan

The statistical analysis is conducted in two phases. The core of the first phase is descriptive; the second phase involves hypothesis testing and model building.

Phase 1 of the analysis describes time use patterns and other characteristics of chronically ill children. This reflects a number of considerations. First, systematic studies of children's out-of-school lives are rare. An analysis featuring tabular data will be well suited to the interests of researchers, practitioners, parents, other readers concerned with chronically ill children, and those who want to learn more about each of the time use domains. Second, the study is the first to measure time use patterns of a large sample of chronically ill children, and is consequently largely exploratory in nature. To ignore the descriptive analysis would require compromising the detail and richness of the data, perhaps leading us to miss some of the important underlying determinants and structure of children's time use. Thus, much of the Phase 2 model building should depend upon insights stemming from exploration of the data during Phase 1.

Phase 2 is initiated for a subject after Phase I is completed for each subset. Phase 2 involves consideration of theoretical models of time use patterns of chronically ill children, particularly those flowing from an ecological system approach. Ecological theory postulates that relations frequently differ by contexts (i.e., interactions among variables are the rule, and it is in these effects that the true complexity of ecological reality will usually be understood).

Phase 2 begins with the testing of a proposed ecological model, but we expect that the model will be changed in light of insights from the Phase 1 analysis and the continuing analysis during Phase 2. Given the exploratory nature of this study, we anticipate that entirely new models will be developed. Our models will frequently involve specifying different regressions for each major family type in the model (analysis of homogeneity of regressions), random as well as fixed factors (mixed models), the simultaneous examination of group and individual effects, and repeated measures of the dependent variables.

Risk-Taking Behavior in Adolescents: Impact of Puberty

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Project Number	MCJ-060564				
Project Period	12/01/87–11/30/90				
Costs*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	150,000	218,236	157,890	n/a	n/a
Requested	198,762	213,173	180,421	n/a	n/a
* Indirect included					

Summary

Statement of the Problem

The purpose of this research is to examine the relationship between timing of physiological development in adolescence and three risk-taking behaviors: Sexual activity, substance use, and injury-related behaviors sustained in recreational vehicles. Adolescence is generally viewed as a period of optimal physical health, yet, in reality, adolescents represent one of the only age cohorts in the United States where mortality is still increasing or remains high. The major causes of morbidity include the consequences of sexual activity, substance use and abuse, and vehicle-related injuries that lead to disability.

Data on the interrelationships among these high-risk behaviors in youth support taking a generic approach to the problem of adolescent risk-taking behaviors. Substance use, sexual activity, and behaviors associated with injuries have high prevalence rates during adolescence and demonstrate strong interrelationships. The most recent prevalence data on these three behaviors show that the age of onset is declining. Although the relationships themselves have been documented, the mediating factors underlying these interrelationships remain unclear.

Our current lack of knowledge about these underlying mechanisms is reflected by our meager progress in affecting adolescent risk-taking behavior. With a better understanding of the mechanisms responsible for the initiation, progression, and maintenance of risk behaviors during adolescence, health professionals will be better able to develop more effective prevention and intervention programs in primary, secondary, and tertiary health care settings for youth at risk for negative health outcomes.

Research Questions or Hypotheses

The underlying hypothesis is that the timing of physiological maturation predisposes adolescents to engage in certain risk-taking behaviors that fulfill critical developmental needs (both psychosocial and physiological) during the second decade of life. Specific psychosocial changes occur along with biological maturation and are associated with adolescent risk-taking behaviors. Timing of biological maturation is expected to directly influence a set of four psychosocial factors: Cognitive scope; self-perceptions; perceptions of the social environment; and personal values. These four factors are expected to influence two mediating factors, peer group selection and perceptions of risk, which, in turn, are hypothesized to predict adolescent risk-taking behaviors.

Self-perceptions, perceptions of the social environment, and personal values are expected to influence the adolescent's choice of a peer group. The adolescent's peer group is then expected to influence risk-taking behaviors, and is hypothesized to be affected primarily by characteristics of the peer group, cognitive scope, and self-perceptions. The influence of personal values on risk taking is expected to occur as a function of its effects on peer group choice, although some direct effects of personal values are also expected.

The study addresses the following hypotheses:

1. Timing of adolescents' pubertal maturation is associated with differences in their perceptions of their early social environment;
2. Timing of adolescents' pubertal maturation is associated with differences in their self-perception;
3. Timing of adolescents' pubertal maturation is associated with differences in personal values, psychosocial maturity, and cognitive capacity;
4. Timing of adolescents' pubertal maturation is associated with differences in risk-taking behavior;
5. Adolescents' environmental perceptions are associated with risk-taking behavior; and
6. Self-esteem is negatively correlated with risk-taking behavior.

Study Design and Methods

The study is a cohort, sequential, longitudinal design, with data collected at three points in time. During phase I of this study, a large cross-sectional sample of adolescents is assessed. In phase II, a cross-sectional subsample of 592 adolescents is extensively assessed. Phase III is the 1-year followup of the phase II subjects.

The adolescents and their parents are asked to give consent to participate in the screening or phase I portion of the study. During phase I, pubertal development and sexual maturation scales are administered, and sociodemographic data and height and weight data are also collected. On the basis of data collected during phase I, subjects are selected for phase II of the study. During phase II, a physical exam, the Marlowe-Crowne Social Desirability Scale, the Jessor and Jessor Scales, and measures of egocentrism, future orientation, body image, risk perception, risk-taking behavior, and environmental perception are administered. Six months after the phase II assessments are complete, phase III followup occurs, and all of the phase II assessments are repeated for phase II subjects only.

Phase I assessments are conducted during one class period. Two other class periods are used for a subject orientation and for a feedback session where each student is given a computer printout of individual pubertal status and an overview of developmental changes that can be expected over the next 1–2 years. Phase II and phase III assessments are conducted at the University of California at San Francisco. Subjects in these last two assessments are paid $10 for each assessment.

Population Description and Sampling Plan

The study sample consists of 1,760 subjects selected from three San Francisco public schools. Two middle schools (subjects selected from grades 6–8) and one senior high school (subjects selected from grade 9) have been selected and have agreed to participate in the study. Approximately 2,100 adolescents are attending the four grades in these schools. Student participation in the study is solicited during required classes to ensure the opportunity for all students at each grade level to participate in the research.

The majority of the students are middle- and lower-middle class, and represent approximately equal numbers of white, black, Hispanic, and Asian backgrounds. This racial and ethnic diversity allows for greater generalizability of study findings. Limiting the sample to no more than four primary ethnic groups leaves sufficient statistical power to detect differences that may emerge. The wide range of ages allows examination of the effects of both early and late physiological maturation, as well as risk-taking behaviors that occur in early or late adolescence.

Analysis Plan

The analysis plan is organized around four tasks: (1) Data reduction; (2) cross-sectional analyses; (3) causal modeling; and (4) longitudinal analyses. Each level of analysis reflects a significant degree of complexity, due primarily to the complex nature of the phenomena under investigation. The analysis takes on an additional level of complexity as a result of its hierarchical structure (i.e., results from early analyses affect subsequent results).

Because of the multidimensional nature of the relationships under examination, the analysis relies primarily on the use of multivariate techniques. This approach not only allows for tests of complex relationships involving multiple dependent and independent variables, but also minimizes the experimental error rate. Univariate statistics are also used when appropriate. Simple and partial correlations are used to evaluate linear relationships between variables. Multiple regression techniques are used to investigate the relationship between multiple predictor variables and a single dependent variable. When variables can be ordered on temporal or substantive grounds, hierarchical multiple regression is used. In cases where mean differences are of interest, analysis of variance is employed. When multiple dependent variables are of interest, multivariate techniques such as canonical correlation or multivariate analysis of variance are used.

LABORATORY EVALUATION OF JAUNDICED NEWBORNS: A REEVALUATION

GRANTEE University of California at San Francisco

INVESTIGATOR

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PROJECT NUMBER MCJ-060573

PROJECT PERIOD 11/01/88–10/31/90

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	99,780	112,766	Denied	n/a	n/a
Requested	103,591	111,146	118,928	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

Jaundice is one of the most common problems of newborns. Most textbooks recommend a series of laboratory tests to investigate the cause of the jaundice. These recommended tests include total and direct bilirubin, blood type and group on mother and infant, a direct Coombs' test, a reticulocyte count, and examination of a peripheral blood smear to evaluate red blood cell morphology. The cost implications of following the current recommendations are substantial: Evaluation of 15 percent of the 3.7 million infants born in the United States each year would cost about $50 million per year. However, the benefits of this strategy are largely unknown because of the paucity of studies addressing the value of the recommended laboratory tests in this setting.

There are good reasons to question the routine use of many of these laboratory tests in jaundiced newborns. First, the prevalence of serious illness in infants who are otherwise well is very low; the burden of subtle disease manifesting itself only as jaundice is very small. Second, the normal or reference ranges for some of these tests are not available for jaundiced newborns. Third, the tests lack sensitivity and specificity for the most treatable illnesses (e.g., sepsis). Thus, true positive results are likely to be much less frequent than false positive results.

The problem, then, is the widespread use of a costly battery of diagnostic tests in jaundiced infants, without previous studies demonstrating that any of these tests are clinically useful, and with good reasons to suspect that they are not.

Research Questions or Hypotheses

This study has the following objectives:

1. Determine the frequency of significant neonatal jaundice (i.e., the frequency of jaundice severe enough that standard textbooks recommend multiple laboratory tests to attempt to evaluate it);
2. Determine how commonly each of the recommended tests is performed for jaundiced newborns at two hospitals;
3. Determine reference ranges at two hospitals for tests commonly ordered to evaluate jaundice in newborns;
4. Determine the frequency of serious illness among patients with abnormal results on these tests; and
5. Use the study results to formulate recommendations for laboratory evaluation of jaundice in term newborns.

Study Design and Methods

This is a retrospective study using several existing computerized data bases, supplemented with chart reviews. The principal data base is the Combined Patient Experience (COPE) data base maintained by the Medical Center of the University of California at San Francisco (UCSF) Department of Laboratory Medicine. The COPE data base is created by merging computer records of clinical laboratory data with computerized medical record, hospital census, and hospital discharge data. COPE includes UCSF data from 1980 to 1982 and from 1986 to 1987, and Stanford University Medical Center data from 1986 and 1987. Other data sources include the UCSF Obstetrics Department data base, the Stanford Hospital Information System, and the Stanford blood bank's computer system.

The data base is used to determine (1) the frequency with which infants exceeded customary thresholds for a hyperbilirubinemia workup, (2) which laboratory tests were actually done, (3) the range of reported results in infants who had other laboratory evidence of disease compared to those who did not have other evidence of disease, and (4) the frequency with which additional tests were ordered to followup on abnormal results. Medical records are examined to obtain long-term followup and to confirm discharge diagnoses.

Population Description and Sampling Plan

The subjects for this study are infants with birthweights greater than 2,500 grams who were born between October 1, 1980, and September 30, 1982, at the University of California at San Francisco, or between January 1, 1986, and December 31, 1987, at either UCSF or Stanford University Medical Center. The sample size for this study is approximately 12,000 newborns for whom data are available in the COPE data base. Although this study focuses primarily on babies who are not critically ill, severely jaundiced infants are not initially excluded from the sample, so that the study will not be biased toward finding that serious consequences of jaundice and useful yields of laboratory tests are rare.

Analysis Plan

Investigation of laboratory data proceeds in two phases. First, simple demographic data (i.e., date of birth, age, sex, race, and birthweight) and results of bilirubin determinations are examined. From this data set, the study ascertains the proportion of babies who have their bilirubin levels checked, the proportion whose bilirubin levels reached 13.0 milligrams per deciliter, and the 95th and 99th percentiles for total and direct bilirubin for babies of each race on each day of life. Of the subset of babies who had one or more bilirubin determinations performed (approximately 60 percent), additional laboratory data are examined.

Specifically, results of laboratory tests generally ordered to evaluate hyperbilirubinemia are analyzed for each patient. This allows the generation of descriptive statistics at different levels of total and direct bilirubin. The hyperbilirubinemia risk factor and analysis begins with descriptive statistics, followed by univariate associations of predictor variables with the presence or absence of any bilirubin value of 13.0 or more. These analyses are followed by stepwise logistic regression with bilirubin greater than 13.0 as the dependent variable. The cost per case of disease detected is estimated for different diseases and different possible diagnostic strategies in order to identify the most efficient strategy. These are estimated separately for various patient characteristics (such as sex, race, and degree of hyperbilirubinemia) related to incidence and prevalence levels of disease conditions. These estimates are crude and subject to underestimation of true costs. However, whatever the limitations of the cost estimates, there is presently a critical lack of data in this area.

PHYSIOLOGIC RISK ASSESSMENTS TO PREDICT PRETERM BIRTH

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PROJECT NUMBER	MCJ-060580
PROJECT PERIOD	10/01/88–09/30/91

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	322,609	419,492	denied	n/a	n/a
Requested	406,797	480,101	321,154	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

This study seeks to (1) validate a highly predictive (retrospective) screening method for preterm birth, using uterine contraction monitoring recently developed by the principal investigator; and (2) determine whether the ability to use this method of identifying women at risk for preterm labor can be further improved by the addition of pelvic examination findings.

Research Questions or Hypotheses

This project addresses two main questions:

1. Can certain physiologic measures (i.e., uterine contraction frequency, cervical examination, and vaginal pH), when determined at standard prenatal visit intervals, be used effectively to identify women who subsequently experience preterm birth because of preterm labor or preterm premature rupture of the membranes (PPROM)?
2. Can interpretation of uterine contraction data be improved and standardized by means of a computer program?

There are four specific hypotheses in the study:

1. Intermittent assessment of uterine contractility for 1 hour at standard prenatal visits during the late second and early third trimesters is an effective means of identifying women without major medical risks who develop preterm labor or PPROM;
2. Periodic examination of the cervix improves the identification of women who subsequently develop preterm labor or PPROM;

3. Abnormally elevated vaginal pH corresponds to a higher risk for subsequent PPROM; and
4. It is possible to develop a computerized interpretation system for the tocodynamometry data, and this system could be broadly replicated as a means of interpreting the uterine contractility data.

The following main questions are to be addressed in the process of developing a computer program to interpret the human abdominal activity monitor strips:

1. Does the baseline drift?
2. Is the signal purely representative of uterine activity or are there other unrelated events to be considered, such as respiration or maternal or fetal movement?
3. Are there different forms of uterine activity that need to be distinguished from each other (e.g., contractures or low amplitude, high frequencv activity and contractions)?
4. If there are different forms of activity, how can they be individually identified and analyzed?

Study Design and Methods

The study design is a prospective, blinded evaluation. Data are collected by three skilled nurse clinicians. Subjects are monitored for 1 hour, using a Termguard–portable tocodynamometer at 24, 28, 30, 32, and 34 weeks' gestation, preceding their usual obstetric visits. At each of these visits, pelvic examinations are conducted, including vaginal pH determinations and cervical examinations.

Women with dilations ≥22 centimeters at the internal os or cervical length ≤30.5 centimeter are sent to the labor floor for further evaluation. Women with cervical change who fail to meet the study criteria for preterm labor are candidates for patient education about the signs and symptoms of preterm labor, weekly clinic visits with cervical examination, and weekly blinded tocodynamometry. No recommendations for bed rest or decreased activity are made. If a patient experiences preterm labor, the data and details are recorded. Only predictive data obtained at least 48 hours prior to admission for preterm labor are included in our analysis. Once a patient is treated with tocolytics, no further predictive data are collected.

Population Description and Sampling Plan

A total of 1,000 women from an ethnically and racially mixed group of clients of a San Francisco obstetric service are being studied. Kaiser-Permanente Hospital provides onsite prenatal care for approximately 1,250 women per year. The population is 21 percent black, 17 percent Asian (mainly Chinese), 8 percent Hispanic (mainly Mexican American), and 54 percent white. Virtually all women receive prenatal care well before 24 weeks' gestation. The extremes of social class are underrepresented in the Kaiser population, since paid health care membership is a prerequisite. The overall preterm delivery rate for women who receive prenatal care at Kaiser Hospital is currently 7–8 percent. Racial differences in the prevalence of preterm and low birthweight infants are apparent, and reflect the relative risks seen in the United States population as a whole. The individual racial and ethnic preterm rates in the Kaiser program, however, are lower than the national rates.

We anticipate that 20 percent of these women will be ineligible to participate and that the excluded group will account for 40 percent of all preterm infants. Exclusion criteria are (1) multiple gestations, (2) history of preterm birth, (3) preterm labor in current pregnancy or before 34 weeks' gestation in previous pregnancy, (4) uterine malformation, and (5) clinical obesity (i.e., >140 percent ideal body weight for height and gestational age by 24 weeks' gestation).

New patients are enrolled until a total of 500 women complete the study. The clinical prediction rule developed with this sample is assessed by application to a second, independent sample of an additional 500 women.

Analysis Plan

In order to establish prediction rules, a descriptive analysis is undertaken to characterize uterine activity, cervical examination findings, and vaginal pH. Inasmuch as pH measurements are logarithmic functions, pH is converted to hydrogen ion concentration prior to any arithmetic manipulation. After appropriate calculations, pH is recalculated. Summary point estimates are identified. These time-specific measures are plotted against time and inspected for gestational age trends. Methods of analysis include repeated measures analysis of variance, Student's *t* test, Wilcoxon-Mann-Whitney test, and logistic regression.

In order to develop a computer program to analyze uterine activity, the study identifies a running mean for the baseline drift in tocodynamometry and subtracts it from the data points, eliminates unrelated uterine noise, and distinguishes forms of uterine activity.

EVALUATION OF THE IMPLEMENTATION OF THE MEDI-CAL COMPREHENSIVE PERINATAL SERVICES

GRANTEE University of California at San Francisco

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PROJECT NUMBER MCJ-067010

PROJECT PERIOD 04/01/89–03/31/92

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	194,039	300,000	300,000	n/a	n/a
Requested	194,039	359,568	366,798	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

The Comprehensive Perinatal Services Program (CPSP) of the California Department of Health Services is the institutionalization of a public perinatal health care demonstration project (OB Access) for low-income pregnant women. This project coordinated nutritional, psychosocial, and health education services with clinical care on a case-by-case basis. Participants in the OB Access project had better birthweight outcomes than those of Medicaid patients with matched demographic risk characteristics who did not receive case coordination and ancillary services. However, because many changes were necessary to implement a comprehensive perinatal service delivery program statewide, the statewide CPSP program might not be as effective as the demonstration project.

The goal of this study is to perform a structure, process, and outcome evaluation of CPSP to determine: (1) How CPSP services differ from both the OB Access pilot project and from Medicaid-paid prenatal care, and (2) whether birthweight outcomes for CPSP are as good as those for the OB Access program and better than those for Medicaid. By studying both services and outcomes, if the birthweight outcomes are indeed better in CPSP than in Medicaid, the characteristics of a statewide comprehensive prenatal care program can be more easily and effectively replicated by others. If there are no differences in birthweight outcomes between CPSP and Medicaid, then the differences between CPSP and OB Access service delivery at provider and patient levels will be characterized so that changes can be made in service organization, content, delivery, and utilization within CPSP in order to improve birthweight outcomes to the level observed in the demonstration project.

Research Questions or Hypotheses

The specific aims of the study are to compare and contrast implementation of CPSP with the OB Access demonstration project and with unenhanced Medicaid perinatal care in four areas: (1) Program administration; (2) provider characteristics and services offered to patients; (3) services received by patients; and (4) birthweight outcomes of infants born to patients.

A research question has been formulated for each specific aim:

1. Program administration: How does CPSP differ from OB Access and Medicaid in administering perinatal care service delivery?
2. Provider characteristics and services offered to patients: How do CPSP providers differ from OB Access and Medicaid providers of perinatal services and how do their services to patients differ?
3. Services used by patients: How does CPSP differ from OB Access and Medicaid care with respect to services used by clients?
4. Birthweight outcomes: How do the low birthweight outcomes of participants in CPSP differ from those of OB Access and regular Medicaid?

Study Design and Methods

To characterize and compare the service delivery systems of the three programs (questions 1 and 2), a structure evaluation is performed. The structure evaluation describes the organizational components of the programs and the care offered. To answer questions 3 and 4, a process and outcome evaluation is conducted to measure and compare utilization of services and birthweight outcomes for the three programs. This component of the study determines the extent to which patients actually receive program services and the associated impact of these services on birthweight outcomes. The evaluation design is technically that of an "after only with comparison group" nonexperimental design. The remaining steps in the evaluation (described below) vary according to the specific research question.

Population Description and Sampling Plan

1. Program administration. All State and county staff responsible for these programs were contacted for interviews.
2. Provider characteristics and services offered to patients.
   a. OB Access providers: All 11 providers were identified from OB Access provider contracts, and data were obtained from documents and reports of the California Maternal and Child Health Branch.
   b. CPSP providers: A survey was conducted of CPSP providers, identified from a list of all certified providers as of October 1, 1989, from the California Maternal and Child Health Branch of the Department of Health Services (231 provider sites).
   c. Medicaid providers: A survey was conducted of a sample of Medicaid providers (physicians and clinics) that did not provide CPSP services.

d. Non-CPSP Medicaid physicians: These physicians were identified from two separate listings of physicians whose primary medical specialty is obstetrics/gynecology or family practice, and who had been paid more than $5,000 by Medi-Cal for services between July 1988 and June 1989.

e. Non-CPSP Medicaid clinics: These clinics were identified from the statewide listing of clinics that meet three criteria: Nonprofit ownership, State licensure, and patient fees scaled according to ability to pay.

3. & 4. Services used by patients, and low birthweight outcomes.

a. Provider Sample: All sites that responded to our CPSP provider survey (174 of 231 provider sites), indicated they had billed CPSP for services already provided by April 1989, and provided CPSP care to at least 50 women a year (89 sites) are included in a sampling procedure of 4 regions comprising more than half the State of California (two metropolitan, two nonmetropolitan regions). The 57 qualifying sites were stratified by 5 types of site (private physician, private hospital clinic, community clinic, public hospital clinic, and public health department clinic). A random sample was sought for the study, to consist of two of each type of site from each geographic region. Because not all types of sites existed in all regions, 29 sites have been selected, comprising seven private physicians, five private hospital clinics, eight community clinics, three public hospitals, and six health department clinics. Only one site (a private physician) refused to participate.

b. Client Sample: The participants in CPSP are low-income, Medicaid-eligible women whose incomes are below 200 percent of the Federal poverty level and whose allowable assets are not to exceed $3,000. At each study site, the birth log or clinic roster of estimated dates of confinement was used to identify CPSP clients with births between June 30, 1989, and December 31, 1990. The medical charts of all women identified from the logs were requested. When a woman was found to have had at least one CPSP clinic visit, one CPSP risk assessment, and a singleton birth within the prescribed time period, then her medical chart, support service risk assessment, and individual case plan forms were abstracted. Each chart that met the above criteria was abstracted sequentially until a total of 140 charts were abstracted at the site. Six sites did not have 140 births that met the criteria, and at those sites the number of charts available for the study varied from 63 to 127. The final sample size for the study is 3,670 women.

Analysis Plan

1. Program administration. The CPSP and OB Access programs are compared qualitatively to outline the administrative changes that occurred during statewide implementation of the pilot project. Issues described include: The range of services offered (benefits); quality assurance of services (certification, audit, and evaluation of program); reimbursement for services and billing procedures; provider relations and recruitment; client recruitment; communications among elements of the program; and qualification requirements for provider staff. In

addition, CPSP and Medi-Cal are compared on these same dimensions to contrast the administration of the comprehensive and regular programs now offered by Medicaid.

2. Provider characteristics and services offered. Information from documents, applications, and provider surveys is collected on the following characteristics of CPSP, OB Access, and Medicaid providers: Provider type (community clinic, private physician, etc.); length of time in obstetrical practice; volume of Medicaid patients; volume of prenatal patients and deliveries performed; ethnicity of patients; geographic location(s) and metropolitan or nonmetropolitan population density of the site location; and relationship with Medicaid.

In addition, CPSP providers and nonparticipating Medicaid providers are asked to name the characteristics of the CPSP program that deterred them from increasing their level of participation or from participating at all.

The way in which OB Access and CPSP providers offered comprehensive services is compared to determine whether there are any differences in the service delivery models utilized. The CPSP program is then compared to regular Medicaid, only with respect to provision of routine obstetrical care services, since Medicaid benefits do not include support services or care coordination.

3. & 4. Services used, and low birthweight outcomes.

Prenatal care services used by patients are analyzed by bivariate analysis of categorical groups for the gestational month of onset of care and proportions of expected visits attended, using the components of the Kotelchuck Prenatal Care Utilization Index generated by the SAS statistical program provided by Dr. Kotelchuck. Our analyses exclude women with no prenatal care or incomplete data for obstetrical visits. Chi-square analyses are performed to ascertain the statistical significance of differences found ($p \leq 0.05$).

Low birthweight outcomes of CPSP participants are compared to those of OB Access and Medicaid participants, using multivariate logistic regression models so that the association between clinical prenatal visits in the programs and health outcomes can be measured while controlling for individual risk characteristics (age, race, parity, marital status, and sex of infant). Chi-square tests are performed to ascertain the statistical significance ($p \leq 0.05$) of associations found.

EFFECTIVENESS OF AN URBAN LOW BIRTHWEIGHT INTERVENTION

GRANTEE The Better Babies Project, Inc.

INVESTIGATOR

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PROJECT NUMBER MCJ-110558

PROJECT PERIOD 10/01/87–09/30/91

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	224,511	229,626	252,440	66,547	n/a
Requested	249,118	257,730	274,530	79,506	n/a

* Indirect included

SUMMARY

Statement of the Problem

The Better Babies Project, an intervention program designed to prevent low birthweight (LBW), was begun by a group of community leaders as a response to the much-publicized problem of low birthweight in the District of Columbia. In 1982, there was great concern in the Washington, DC, community about the high rate of infant death and low birthweight deliveries. City public health and medical services were attempting to address the problem in several ways, mostly by focusing on prenatal care. Little was known about the impact of these efforts on birth outcomes. Somewhat less attention was being paid to prenatal care access or to efforts to enhance prenatal care as described in the Institute of Medicine's 1985 report on the problem of low birthweight.

The present study is designed to test the impact of a particular community-based approach to enhanced prenatal care on the birthweight of infants born to African-American women residing in relatively poor and ethnically segregated neighborhoods. In light of the current interest in community-based approaches to the problem of low birthweight, the study uses a set of analyses to examine the impact of the intervention on the community's birth outcomes as well as on the sample of women who participate in the intervention. This study differs from previous work in several ways: (1) It examines an intervention approach offered in a free-standing drop-in center rather than hospital or home-based sites, (2) it systematically examines the impact of quantitative estimates of the level of intervention participation for each delivery, and (3) it uses a comprehensive LBW/prematurity risk factor assessment approach for a sample of women across the LBW risk spectrum.

Research Questions or Hypotheses

We hypothesize that women living in the geographic area where the intervention is offered will have significantly lower rates of LBW deliveries than women living in a matched comparison area. In addition, we are interested in exploring the following research questions: What is the impact on birthweight and gestational age (separately and jointly) of LBW risk characteristics and of intervention participation? What are the effects of age and LBW risk characteristics on intervention participation and on birth outcomes? What is the impact of recruitment methods on intervention participation and on birth outcomes? What are the stress and social support characteristics of this sample of low-income African-American pregnant women? What is the impact of intervention participation on risky health behavior in this sample?

Study Design and Methods

Services are offered in one target neighborhood for 3 years, following an 18-month pilot test of these services, so that we can compare the community's rate of low birthweight following this trial with its rate prior to the trial and with the rate of a comparison area in the city. Random allocation of participants to a treatment group and a control or comparison group is not possible in this trial for ethical, social, and political reasons. This time series, nonequivalent comparison group design is a stronger test than a simple pretest/posttest intervention design because it reduces to some extent the selection bias inherent in the pretest/posttest design. Our goal is to reduce the rate of low birthweight in this community by 20 percent over the 3-year period. This means that, if we can recruit half of all delivering women in the target area, we would have to reduce the rate for participants by about 40 percent. We want to include nonparticipants as well as participants in our outcome criteria goals because this might reduce selection bias.

Women who are living in nine geographically contiguous census tracts in northeast Washington, DC, and who are served by the same health care services are aggressively recruited to participate in an intensive health education intervention. This intervention includes social and material support; smoking, drug, and alcohol cessation sessions; and health education about the risks of low birthweight and preterm delivery. Services are offered by lay health educators under the supervision of a nurse and social worker, through a neighborhood drop-in center, and (for some women) through limited home visits. The women's low birthweight risk and intervention participation are assessed at least monthly. These risk assessments are used to develop individualized service plans, and specific data are collected on the participation of each subject, using a participant-observer instrument. Standardized assessment instruments enable staff to offer individualized services to women in an appropriate manner and to document these services. At first contact, an information form is used to determine whether a woman is in prenatal care, and to ascertain the gestational age of the fetus and her plans for prenatal care.

Women who participate in the intervention are interviewed, and their current pregnancy experiences and pregnancy and health history are recorded on an information form. This needs assessment information is used to develop each woman's LBW risk factor profile and to identify which women are at risk for particular risk factors.

Additional measures document planned services and actual services provided to each woman participating in the intervention. These measures are easy to use and help staff to assess the major LBW risks, record each woman's individual needs and the number of actual services received, and reassess women at each monthly interval, at delivery, and at approximately 6–8 weeks postpartum. The measures have high face validity and had test-retest reliability indices in the moderately high range ($r = .68$ to .88). A detailed description of the procedures used to offer each risk-reduction service component and copies of measures used to collect risk and participation data are available from the project director.

In addition, we developed a personal computerized case management system to assist each lay health counselor and her supervisor in managing a caseload. This system assists the staff in offering consistent, individually tailored services to a large number of women with diverse needs. Information on these methods is available from the project director.

Since neither interventions nor participants were randomized, we do not have an ideal comparison group. We used aggregate vital records data to construct a reasonable comparison group. Census tracts in the District of Columbia with a predominance of births to African-American women and an equivalent low birthweight rate are chosen as potential comparison census tracts. We then compare maternal age, education, marital status, obstetric history, and birth Apgar scores for women living in the target area to the potential comparison census tracts for the years 1980–1985. Although the low birthweight rate in the comparison census tracts was slightly higher (16.5 percent compared to the target area rate of 15.3 percent), there was no significant difference between the two ($X^2 = 2.7$, $p = .1$). Similarly, there are no significant differences, using vital records data, between the target and comparison area for any of the other important correlates of low birthweight.

Population Description and Sampling Plan

The target neighborhood is primarily low-income (about 31 percent below the Federal poverty level), with about 6,200 residents of childbearing age, a consistently high rate of LBW deliveries (15 percent), and an average of 547 births annually. Based on this, we anticipated approximately 1,640 births in the target neighborhood during the study period, and we hoped to recruit 80 percent, or 1,313 women. According to actual vital records data, 1,784 births occurred, an 8 percent increase over our estimate. (One factor that may have contributed to the higher birth rate was the congressional ban during the study period, prohibiting the District of Columbia from using either Federal or local funds to assist poor women seeking abortions.)

We recruited 1,061 women from the target area during the trial. This is 80.1 percent of our original goal, or 65 percent of the estimated number of women expected to deliver. Because the total number of births was higher than expected, our number of recruits, in fact, equaled only 60 percent of the total number of births. We used monthly and yearly enrollment goals to achieve our recruiting objectives. Recruiting the sample was labor intensive and difficult. Additional data on our outreach efforts are available from the project director.

Analysis Plan

Two statistical approaches are used to address the research hypothesis and questions of interest. Both between-group and within-group analyses are used. To address the research hypothesis concerning a reduction in the LBW rate in the community, log linear analyses are used to compare the rates of low birthweight and of very low birthweight for the service neighborhood and the matched comparison area.

The research question regarding the joint impact of risk and intervention participation on birth outcomes is addressed by an analysis of four primary factors: Birthweight (BW), gestational age at delivery (GA), severity of each woman's assessed risk, and intensity of the actual intervention. The type of intervention a woman receives depends upon many factors, including the intended intervention and her compliance with these plans. Her compliance is, in turn, related to her risk. In this naturalistic framework, risk is divided at the median score and risk level is used as a stratifying factor in the analyses. The relationship of risk to actual intervention is also examined. Furthermore, while there is a complex relationship of birthweight to gestational age at delivery in small or premature infants, the two quantities are highly correlated ($r = 0.64$, $p < .0001$). This relationship is also considered in the analyses.

Statistical tests are based on categorical versions of all four variables. Both risk and intervention are divided into two categories at their median scores. Birthweight is divided into the traditional categories of normal ($\geq$2,500 grams), low ($\geq$1,500 and $<$2,500 grams), and very low ($<$1,500 grams). Gestational age at delivery is also divided into three categories: Normal ($\geq$37 weeks), short ($\geq$32.5 and $<$37 weeks), and very short ($<$32.5 weeks).

Initially, we used a log-linear model to test the hypothesis that, conditional upon risk level, intervention was independent of the joint distribution of birthweight and gestational age. As a check on the validity of our risk score, a model relating risk (conditional upon intervention) to birthweight and gestational age was also examined. This form of the log-linear model treats the variables as nominal and thus is insensitive to the direction of the results. The study also uses an alternative analysis that emphasizes normal birthweight and normal gestation, and assigns row, column, and joint weighing factors to each of the 3 × 3 tables of birthweight by gestational age.

The remaining research questions are examined using chi-square and regression analyses. Analyses that examine the impact of intervention on changes in risk behavior examine behavior across time, as assessed at monthly intervals, to develop change scores. Differences in change scores for various subsamples of women at risk for various LBW risk factors are examined using chi-square analyses.

INTERACTION AND SUPPORT: MOTHERS AND DEAF INFANTS

GRANTEE	Gallaudet University
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PROJECT NUMBER	MCJ-110563
PROJECT PERIOD	10/01/87–09/30/90

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	154,894	158,349	142,052	n/a	n/a
Requested	198,077	200,000	175,000	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

Deaf children with hearing parents are known to be at risk for language delays, academic underachievement, and emotional-behavioral disorders. Early intervention increases performance levels, but difficulties in detecting congenital deafness have delayed application of audiological and educational expertise. Recent advances in diagnostic procedures and practices mean that more infants are identified early, but little research has been done on the developmental impact of early hearing loss. Thus, current intervention techniques with deaf infants are not based on developmental research with infants, since little is known about this population in the first year of life.

This research is designed to investigate the impact of hearing auditory loss on early mother-infant interaction, on infants' motivation to master the environment, their social coping skills, and their communication development. These developmental domains are viewed in the context of the family stress created by the diagnosis of deafness and the network of social support available to parents.

Research Questions or Hypotheses

Based on earlier research with deaf toddlers, it is hypothesized that, compared to hearing infants, deaf infants of hearing mothers will have problematic social interactions with their mothers and delayed language acquisition or prelinguistic skills. It is assumed that deafness will not influence infants' motivation to explore objects in the environment, provided cognitive and physical skills are intact.

It is further hypothesized that mothers of deaf infants will be less likely to provide appropriate visual and social stimulation to their infants, compared to mothers of hearing infants.

An important research question is the extent to which social support for mothers of deaf infants can buffer or mediate the stress of the diagnosis of deafness, improving mothers' interactive skills with observable effects on deaf infants' functioning in mastery motivation, social coping and interaction, and communication.

Study Design and Methods

Pilot research has demonstrated the difficulty of locating deaf infants before 9 months of age. Therefore, four research groups have been invited to assist the Gallaudet investigators in recruiting subjects and collecting data. (These groups have access to appropriate laboratories and equipment, and are located at the University of Texas, Dallas; Georgia State University, Atlanta; University of Pittsburgh; and University of Massachusetts, Amherst.) Data are to be collected on infants at 9, 12, 15, and 18 months of age. The 15-month contact is a home visit for the purpose of interviewing the mother; other data are collected in a laboratory at one of the five research sites.

At the 9-month visit, mothers and infants are videotaped in a standard face-to-face interaction format (Brazelton/Tronick), with two 3-minute intervals of normal interaction separated by a 2-minute still-face episode where mothers are instructed to be nonresponsive. Mastery motivation is assessed by presenting four age-appropriate toys, following procedures developed by Yarrow's group at the National Institutes of Health. An interview is conducted and data are collected on family stress and support, using Abidin's Parenting Stress Index and a Stress of Life Events questionnaire.

During the 12-month visit, mastery motivation is assessed a second time; mothers and children participate in a 15-minute unstructured play session, and in the Ainsworth Strange Situation, a standard laboratory procedure for assessing infants' attachment to their mothers through a series of brief separations and reunions.

At 18 months, mothers and children are again engaged in the Strange Situation and in 20 minutes of free play. Another interview is conducted and additional questionnaire data are collected on parenting stress and family support, using the Parenting Events Inventory and Family Support Scale.

Population Description and Sampling Plan

The study recruits 20 normally developing, hearing-impaired infants from 5 metropolitan areas; infants with normal hearing are matched with the deaf infants for gender and mother's education. Infants' hearing losses are sensorineural and in at least the moderate range. It is expected that families will be mostly white, middle class, and college educated, but subjects are not excluded because of race, ethnicity, or socio-economic class. All babies within the five metropolitan areas who are diagnosed as deaf but who have no additional handicaps are recruited. Extensive contacts with medical, audiological, and educational service professionals are organized by each research group, in an effort to initiate referrals to all newly diagnosed infants.

Analysis Plan

Each data set is analyzed separately, coded from videotapes or from transcribed audiotapes of interviews. The Monadic Phase coding system, developed by Brazelton, Tronick, and colleagues, is modified for use with this population and used for face-to-face interaction data collected at 9 months. Coding systems developed by Yarrow, MacTurk, and colleagues are used for mastery motivation data.

Communication/language codes and global rating scales are developed by project staff for mother-child interaction during free play at 12 and 18 months. Indices reflecting family stress and support are developed from the four questionnaires completed by parents when their infants are 9 and 15 months of age.

Cross-sectional data analyses comparing deaf and hearing infants and their mothers at each of three age points are conducted by means of *t* tests or analyses of variance and correlations. Where appropriate, multivariate analysis of variance techniques are used. Stress and support indices are defined as mediating variables. Independent measures summarizing mastery motivation, social skills, and coping skills will be constructed from those data sets. Two step-wise multiple regressions are computed, using the 18-month dyadic global ratings and the 18-month infant communication measures as dependent variables.

REDUCING THE NATION'S PEDIATRIC INTENSIVE CARE MORTALITY

GRANTEE Children's National Medical Center

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PROJECT NUMBER MCJ-110584

PROJECT PERIOD 04/01/89–03/31/93

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	193,687	386,455	230,914	207,095	n/a
Requested	193,687	429,394	230,914	207,095	n/a

* Indirect included

SUMMARY

Statement of the Problem

Quality assessment is an increasingly important issue for our health care system. Intensive care is a significant component of this system, not only because technologically sophisticated care benefits many patients, but also because, as the most sophisticated hospital care routinely available, it demonstrates our general commitment to health care. No efforts have been made, however, to determine the specific characteristics of pediatric intensive care that are associated with good outcomes. This is an especially important issue in the current organization of intensive care units. There is a proliferation of pediatric intensive care unit (PICU) services in all types of hospitals, but little is known about which characteristics of intensive care are associated with quality of care.

Data indicate that quality of care may differ substantially among intensive care units. A recent statewide study demonstrated that quality and outcomes of pediatric intensive care differ among intensive care units with differing characteristics. Quality of care was assessed by comparing the number of observed outcomes to the number of expected outcomes and by comparing mortality rates (adjusted for severity of illness) from one set of institutions to another. Tertiary and nontertiary hospitals were studied. In patients admitted to tertiary care centers, the observed outcomes were similar to the number of expected outcomes, using a validated severity of illness method, the Pediatric Risk of Mortality (PRISM). However, the number of deaths among patients admitted to the nontertiary center was higher than expected. The most severely ill patients are six times more likely to die in a nontertiary care center than in a tertiary center (odds are adjusted for severity of illness).

This study is designed to ascertain which characteristics of pediatric intensive care units and their hospitals determine the quality of care. The study characteristics include size, medical school teaching status, intensivist status, and coordination of care among multiple care teams

Research Questions or Hypotheses

We hypothesize that the relationship of physiologic instability (severity of illness as assessed by the PRISM score) to outcome (survival or death) is dependent on specified care characteristics, including size ($\leq$ 6 beds versus $>$ 6 beds), medical school teaching hospital status (primary versus secondary teaching status), pediatric intensivist status (present or absent), and coordination of medical care (present or absent). Lack of coordination of care is defined by the absence of medical director involvement in care and lack of a physician team dedicated to the PICU.

Study Design and Methods

A national survey of known pediatric intensive care units establishes the frequency of each of the variables specified in the hypothesis. Survey responses are confirmed by telephone. Pediatric intensive care units that are eligible for the study (i.e., those responding to the survey, large enough to accumulate 15 deaths over 24 months, willing to participate, and whose status is stable with respect to the study characteristics) are stratified into 16 groups, using unique combinations of the study variables. One PICU from each of the strata is selected randomly to be visited by the principal investigator. Pediatric intensive care units that do not meet the study requirements are replaced by another unit chosen randomly.

Telephone surveys are conducted of PICUs that do not respond to the mail survey. Questions are similar to those asked of the original sample. This group of PICUs is compared to the volunteer units for their intensive care unite characteristics, including the study characteristics and other data available from the American Hospital Association.

Each participating PICU is site-visited to confirm the study characteristics and to teach data collection techniques. Data are collected on consecutive admissions at each PICU, including physiologic data and descriptive data (age, diagnoses, operative status, chronic diseases, functional status, therapies administered, clinical physician services, participation in patient management). Descriptive data are compiled at participating institutions. Physiologic data consist of information from the bedside cardiovascular and neurologic vital sign sheets and the laboratory reports. PICUs submit photocopies of this information for the first 32 hours of intensive care unit care. Specifically, the following laboratory variables are used: Heart rate, respiratory rate, systolic blood pressure, diastolic blood pressure, coma status, pupillary reflexes, potassium, calcium, bilirubin, glucose, serum bicarbonate, prothrombin time, partial thromboplastin time, PCO_2, and PaO_2/FiO_2. This information is computerized.

Each patient is described by study characteristics, age, operative status, diagnosis, physiologic status, and outcome. Physiologic status is summarized using the PRISM score. PRISM utilizes the physiologic variables specified above to estimate mortality risk based on the clinical importance of the physiologic derangement.

Population Description and Sampling Plan

The study involves 16 randomly selected PICUs representing the 16 unique combinations of the study characteristics specified in the hypothesis. Each PICU collects data on consecutive patients until 15 deaths have been accumulated. Patients remaining in the PICU when the 15th death occurs are also included. It is expected that a total of 500–600 patients will be enrolled, although institutional samples may vary from 100 to 700.

Analysis Plan

The statistical evaluations comparing the two samples of PICUs include Hotelling's T^2-test for two group multivariate analysis of variance, and univariate analysis by *t* tests, analysis of variance, chi-sqaure analysis, and Fisher exact test. The Bonferroni adjustments for alpha error are made when post-hoc univariate comparisons are made following the Hotellings T^2-test.

Analysis of the central hypothesis includes a stepwise logistic regression model predicting PICU outcome from PRISM scores with the care factors as covariates. The statistical significance of these care factors is assessed by the likelihood ratio statistic. These results are confirmed with secondary analyses including goodness-of-fit tests and Flora's method based on the *z* statistic.

IDENTIFICATION OF RISK FOR SIDS: SUBSEQUENT SIBLINGS

GRANTEE American Sudden Infant Death Syndrome Institute

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PROJECT NUMBER MCJ-130516

PROJECT PERIOD 04/01/85–03/31/90

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	131,156	108,925	125,251	139,788	130,954
Requested	150,812	127,812	135,925	140,376	136,586

* Indirect included

SUMMARY

Statement of the Problem

This research project is part of a larger program to develop a clinically applicable procedure for early identification of infants at increased risk for dying of sudden infant death syndrome (SIDS). It is a direct outgrowth of the current medical management for a group of infants known to be at increased risk for SIDS: Infants (subsequent siblings) who are born into families that previously lost a baby to SIDS.

Determining which subsequent siblings should be provided with home monitoring is a fundamental problem faced by those who direct the clinical management of these infants. There are two general approaches to this problem. One approach recognizes that currently there are no valid means for differentiating those subsequent siblings who are truly at risk from those who are not. Clinical groups who accept this premise either recommend home monitoring for all subsequent siblings or recommend that no subsequent sibling be treated with home monitoring.

Other groups, finding this all-or-none approach unsatisfactory, base their recommendation on the results of a clinical history, physical examination, discussions with parents, and selected screening test procedures (usually a pneumocardiogram). Unfortunately, none of these criteria are based on substantial scientific evidence. As a consequence, the overall clinical management of subsequent siblings tends to be arbitrary, confusing, and unnecessarily expensive.

Nonetheless, a growing body of knowledge indicates that there are manifestations in the neonatal period indicative of risk status for SIDS, and that physiological observation of feeding and sleep (under carefully controlled conditions) and assessment of muscle tone might provide objective, valid criteria for early identification of those subsequent siblings who would benefit from home monitoring. The primary purpose of this study is to evaluate the effectiveness of these objective clinical approaches to risk identification when used in subsequent siblings.

Research Questions or Hypotheses

The primary objectives of this study are to:

1. Determine the proportion of subsequent siblings who develop episodes of prolonged apnea and/or bradycardia;
2. Test the hypothesis that neonatal respiratory instability during sleep and/or feeding and muscle hypotonia are associated with the occurrence of prolonged apnea and/or bradycardia; and
3. Determine the effectiveness of measures of respiratory instability during sleep and/or feeding and muscle hypotonia—considered separately and in combination—in identifying subsequent siblings at risk for prolonged apnea or bradycardia.

Additional objectives include an indirect examination of:

4. The hypothesis that respiratory instability during sleep and feeding and muscle hypotonicity are neonatal manifestations of the same underlying abnormality; and
5. The assumption that episodes of prolonged apnea and/or bradycardia are a surrogate for SIDS.

Study Design and Methods

All subjects included in this study were born to parents who had previously lost a baby to SIDS (with diagnosis confirmed by autopsy). These infants are seen within the first 10 days of life at the American Sudden Infant Death Syndrome Institute (in Atlanta, Georgia, or Portland, Oregon). During this visit and subsequently during the fourth postnatal week, several measurements are obtained from these infants in a controlled laboratory during feeding and during sleep. In addition, muscle tone is evaluated during the clinical examination.

Parents are taught to use an impedance-type apnea/bradycardia monitor, an event recorder, and resuscitative techniques. The event recorder saves on a floppy disk the respiratory and electrocardiogram (ECG) waveforms as well as the instantaneous heart rate 30 seconds prior to and 10 seconds following each violation of the event recorder or monitor settings. Parents are asked to mail these disk recordings to the institute bimonthly, where they are processed to provide a visual display of the respiratory and ECG waveforms and the instantaneous heart rates associated with each violation of the settings. When apnea is suspected, the respiratory signal is amplified further. It is intended that these infants be monitored for at least 6 months.

Population Description and Sampling Plan

Participants were recruited through mass mailings to obstetricians, pediatricians, and general practitioners in Georgia, Oregon, and surrounding States and through public service announcements on radio and television. Using these methods, we recruited 199 subjects. Infants who had one parent in common with a sibling who died of SIDS were excluded. To be included in the study, infants also had to be available for an initial laboratory study within the first 10 days of life.

Subjects were omitted from the analyses if they failed to complete the battery of neonatal test procedures ($N = 10$), if home monitoring was discontinued before completion of the followup period ($N = 25$), or if there was an extended period (≥ 4 weeks) when the recording equipment did not function or was not used ($N = 8$). One infant (while not on a monitor) died of SIDS within the first month of life.

Analysis Plan

The analysis of the data proceeds as follows:

Objective 1: The percentage of infants who develop apnea episodes of varying duration (≥ 15, ≥ 16, ≥ 17, ≥ 18, ≥ 19, and ≥ 20 seconds) are calculated for each age period separately and across the entire study period. The same analyses will be conducted for bradycardia of varying duration (≥ 5, ≥ 6, ≥ 7, ≥ 8, ≥ 9, and ≥ 10 seconds). Several types of bradycardia (≥ 5 seconds in duration) are considered separately: (1) All heart rates included in the episode are below the low heart rate setting; (2) one or two of the instantaneous heart rates within the episode are above the low heart rate setting; (3) an episode is associated with an erratic respiratory pattern; (4) an episode is preceded by a high amplitude respiratory cycle and followed by apnea; and (5) an episode is associated with periodic apnea.

Changes across the five time periods are evaluated statistically by calculating Cochran's Q for repeated measures and comparing this computed value with the tabled chi-square value with 4 degrees of freedom. Proportions for adjacent time periods are compared when the computed value for Q exceeds the tabled chi-square at the 0.05 level.

Objective 2: Measures of neonatal respiratory instability during sleep or feeding are dichotomized into normal or abnormal, based on values derived from a large population of infants who were studied to obtain normative data. The association between these measures of instability and the occurrence of apnea or bradycardia are tested using a Fisher's exact test. Fisher's exact tests are also used to test the association between muscle hypotonia (scarf sign, shoulder girdle tone, trunk extensors, trunk flexors, popliteal angle, and adductor angle) and the occurrence of apnea or bradycardia.

Objective 3: The specificity and sensitivity of various laboratory measures in predicting prolonged apnea and/or prolonged bradycardia are calculated.

Objective 4: Tests of association (chi-square or Fisher's exact) are conducted between the various measures of muscle tone and the various measures of respiratory instability to examine the hypothesis that respiratory instability during sleep and/or feeding and muscle hypotonia are neonatal manifestations of the same underlying abnormality.

Objective 5: To indirectly examine the assumption that episodes of prolonged apnea and/or prolonged bradycardia are surrogates for SIDS, a number of maternal and obstetrical variables are compared between those infants who had apnea or bradycardia and those who did not. Categorical variables are examined with chi-square tests of homogeneity and continuous variables are analyzed with *t* tests.

AN EDUCATIONAL BEHAVIORAL PROGRAM FOR PKU

GRANTEE University of Illinois at Chicago

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PROJECT NUMBER MCJ-170575

PROJECT PERIOD 11/01/88–10/31/91

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	117,116	146,679	110,774	n/a	n/a
Requested	156,788	162,977	119,601	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

The purpose of this study is to determine whether participation of school-age children with phenylketonuria (PKU) in an educational behavioral program will result in improved metabolic control. Metabolic control in this population is important because many patients with PKU who discontinue diet therapy at age 6 experience a decline in school achievement and intellectual performance, and women with PKU must adhere to a phenylalanine-restricted diet during pregnancy in order to prevent the maternal PKU syndrome.

We developed a program that uses an educational and behavioral approach for different age groups of PKU patients. This program is designed to: (1) Increase participants' knowledge about PKU, including the implications of PKU for reproduction; and (2) foster self-reliance in the management of PKU. We anticipate that the results of this study will be instrumental in developing strategies for the long-term management of PKU and in preparing patients for self-management throughout adult life.

Research Questions or Hypotheses

The purpose of this study is to: (1) Determine whether participation in the educational program results in increased knowledge about PKU; (2) determine whether participation improves metabolic control; and (3) identify parameters that will predict success with the program.

Study Design and Methods

This study employs a two-period crossover design, with each period lasting 1 year. Each subject receives two treatments (experimental and standard), with the order of treatment determined randomly. This gives all subjects the opportunity to receive the experimental treatment. In a crossover trial, subjects serve as their own controls, and thus the sample size required is smaller than that needed for a conventional randomized trial. One of the assumptions of a crossover design is that there is no carryover effect. However, we hope that, in this study, the effects of the intensive intervention of the experimental treatment will endure beyond the short term, and we will attempt to determine whether there is any carryover effect.

Since the number of subjects is small, restricted randomization is needed. The subjects are divided into four strata according to sex and age group. Within strata, random permuted blocks of size four are used to determine treatment assignment.

At the first session, the following data are collected from patients who agree to participate in the study: Blood phenylalanine, knowledge of phenylketonuria, IQ, school achievement, psychopathology, cognitive maturity, locus of control, family environment, and social maturity. Subjects in the control group receive standard care. This includes two or three clinic visits per year, when a blood sample and diet record are collected and progress and problems with the diet are discussed. Between clinic visits, the parent and/or patient mails blood samples to the clinic at monthly intervals, along with 3-day diet records. After blood analysis is completed and dietary intake is calculated, the parent or patient is notified and the dietitian adjusts the diet (by telephone contact).

The experimental group is involved in an educational and behavioral program that includes setting behavioral goals and self-monitoring. The educational sessions are held at 4-month intervals, beginning with the first clinic visit. At this session, behavioral goals are set, focusing on some or all of the following target behaviors: Mixing and drinking a phenylalanine-free formula daily, avoiding high protein foods, eating allowed foods in specific quantities, eating low protein foods daily, keeping a food diary or checklist, and taking and sending frequent blood samples. Activities to increase patients' knowledge of PKU are initiated at this session.

Between educational sessions, the experimental subjects are expected to send a blood sample, a diet diary, and completed homework on a biweekly basis. The diet diaries are completed by the patients in the two older age groups, and servings of low phenylalanine foods eaten are tallied by the patients in the youngest age group. Points are awarded biweekly for each blood sample, diet diary, and completed homework assignment. The number of points earned are subtotaled at each clinic visit and small rewards are given for those who earn at least 60 percent of the points.

At the last session, measures given at the first session are repeated. At this time, experimental subjects cross over and become control subjects and the controls cross over and become experimental subjects.

Population Description and Sampling Plan

Subjects ranging in age from 6 to 18 years are recruited from the PKU clinics at the University of Illinois Hospital at Chicago and the Children's Memorial Hospital. All subjects have PKU, a normal IQ, and are currently treated by diet. Subjects learn about the nature of the study and sign informed consent forms; confidentially is maintained.

Analysis Plan

1. Between-group analysis: To determine whether the change in knowledge of PKU is significantly different between the experimental group and the control group, an analysis of covariance (ANCOVA) is performed. There are two age groups: Children ages 6–11 years who require parental assistance, and adolescents capable of independence. Age group and baseline knowledge are used as covariates. Because of a likely carryover effect in the subjects who receive the experimental treatment first, only the data from the first period of the crossover design is used. Subjects who receive the experimental treatment first cannot serve as true controls in the second period since it is likely that their knowledge of PKU will have stabilized by the end of the treatment period and no further improvement will occur over the followup period. In contrast, those subjects who serve as controls first may show some gain in knowledge from the standard treatment.

   Similar ANCOVAs are performed to test for a significant difference between the experimental group and control group with respect to the change in blood phenylalanine level, IQ, school achievement, psychopathology, cognitive maturity, locus of control, family environment, and social maturity.

2. Within-group analysis: To determine whether knowledge of PKU is significantly increased from its baseline measure, an ANCOVA is performed using only the data for subjects receiving the experimental treatment. Age group is used as a covariate to account for possible differences in the change of knowledge between preadolescents and adolescents. Baseline knowledge of PKU is also used as a covariate to adjust for any regression to the mean effect. A similar analysis is performed to test for a significant change in the blood phenylalanine level.

   In addition, a logistic regression analysis is carried out to assess whether baseline measures such as knowledge of PKU, IQ, school achievement, psychopathology, cognitive maturity, locus of control, family environment, and social maturity are predictors of success in completing the treatment program. Again, age group is treated as a covariate to adjust for possible differences between preadolescents and adolescents.

   Finally, for the experimental subjects who complete a 1-year followup period, an analysis of covariance is executed to test whether their blood phenylalanine level is maintained to the end of the followup period. Blood phenylalanine is a good indicator of dietary compliance. Age group and baseline blood phenylalanine level as measured at the end of the treatment period are used as covariates. Similar ANCOVAs are performed to see whether there are any changes in IQ, school achievement, psychopathology, cognitive maturity, locus of control, family environment, and social maturity.

NATURE, ORIGINS, AND CONSEQUENCES OF CONCEPTIONS OF PARENTING

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PROJECT NUMBER	MCJ-190572				
PROJECT PERIOD	10/1/88–09/30/90				
COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	114,404	118,367	n/a	n/a	n/a
Requested	118,466	126,111	n/a	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

Several researchers have called upon their colleagues in behavioral science to investigate the impact of cognitions upon parental behavior. Research on the connection between parents' ideas and parenting behavior has been discouraged, at least in part, by the fact that studies to date have often found either no association or only a very modest relationship between the two phenomena.

These unexpected and inconsistent findings might be viewed, however, as a consequence of the rather simple assumptions that researchers have often made concerning the association between parental cognitions and behavior. There is a need for studies that utilize theory to identify the ideas that are most likely to be consequential and the dimensions of parental behavior that are apt to be affected by these cognitions.

Research Questions or Hypotheses

This study has a two-part strategy. First, social learning/exchange principles are used to generate hypotheses regarding the types of parenting beliefs that influence parenting practices, and the relationship of these beliefs to other factors that have been found to affect parental behavior. Thus, the first part of the study develops a multifactor, causal model of the determinants of parental behavior, with parenting beliefs constituting a component of the model. The second part of the study involves formulating and testing hypotheses concerning the manner in which parenting beliefs are learned. This portion of the study examines the extent to which beliefs about parenting are transmitted across generations.

Specific hypotheses tested include the following:

1. Mothers and fathers who find interaction with their child to be quite satisfying are likely to engage in supportive parenting while eschewing harsh discipline, whereas parents who report little enjoyment from the parent-child relationship will manifest low levels of supportive parenting and high levels of harsh discipline.
2. A wife's degree of satisfaction with the parent-child relationship is positively related to her husband's degree of supportive parenting and inversely associated with his level of harsh discipline.
3. Parents who believe that parenting practices exert a strong influence on child development are more apt to engage in supportive parenting than are parents who do not have such beliefs.
4. There is a positive association between a mother's belief that parenting is a determinant of child development and her husband's level of supportive parenting.
5. Mothers and fathers who perceive physical discipline to be efficacious engage in higher levels of harsh discipline than parents who believe that induction and reinforcement are the most effective approaches to child management.
6. A childhood history of exposure to harsh discipline is positively associated with depression among mothers and fathers, and a history of exposure to supportive parenting is negatively associated with depression among mothers and fathers.
7. The impact of depression on parenting is mediated by the level of satisfaction with the parent-child relationship.
8. Exposure to supportive parenting as a child is associated with beliefs that parental behavior has a major impact on child development, whereas exposure to harsh discipline as a child is related to beliefs endorsing corporal punishment as a method of child management.
9. Mothers and fathers exposed to supportive parenting as children are more likely to report satisfaction with their child than parents who did not receive supportive parenting.
10. Even after controlling for emotional state, depression, and satisfaction with the child, exposure to supportive parenting as a child is a predictor of current level of supportive parenting, and exposure to harsh discipline as a child is a predictor of current level of harsh discipline.
11. Education is positively associated with supportive parenting and negatively related to harsh discipline.

Study Design and Methods

Data are collected from families when the target children are in seventh grade and, again, a year later in eighth grade. Essentially the same procedures and instruments are used at both data collection points. Both waves of data collected involve two visits to each family. During the first visit, each of the family members completes a set of questionnaires focusing on family processes, individual family member characteristics, and economic circumstances. Between the first and second visits, family members

181

complete questionnaires left with them by the first interviewer. These questionnaires deal with information concerning the parents' parents, beliefs about parenting, and plans for the future.

During the second visit, which normally occurs within 2 weeks of the first, the family is videotaped while engaging in several different structured interaction tasks. The visit begins by having each individual complete a short questionnaire designed to identify issues of concern or disagreement within the family (such as chores, recreation, or money).

For the first interaction task, the family members are gathered around a table and given a set of cards to read and discuss. All family members are asked to discuss among themselves each of the items listed on the cards and to continue talking until the interviewer returns. The items on the cards concern family issues such as discipline, chores, and the children's friends and school performance. In the second task, the family is asked to discuss and try to resolve the issues and disagreements which they cited in the questionnaires they completed earlier in the visit. In the third task, the children are given a set of cards listing questions related to the way they get along, the manner in which their parents treat them, their friends, and their future plans. In the fourth task the married couple is asked to discuss issues related to aspects of their relationship, areas of agreement and disagreement (such as parenting or finances), and their plans for the future.

During the time when they are not involved in a videotaped interaction task, each family member completes an additional questionnaire asking about significant life events, attitudes toward sexuality, and personal characteristics.

The videotapes are coded by project observers using the Iowa Family Interaction Rating Scales, which focus on the quality of behavior exchanges between family members.

Population Description and Sampling Plan

A sample of 451 two-parent families was recruited from the cohort of all seventh grade students, male and female, who were enrolled in public or private schools in 8 counties in north central Iowa during the winter and spring of 1989. An additional criterion for inclusion in the study is the presence of a sibling within 4 years of age of the seventh grader. Slightly less than half of the cohort of seventh graders had families who met these criteria; 78 percent of the eligible families agreed to participate in the study. Families receive $250 for their effort, which is the equivalent of about $10 per hour for each family member's time.

Approximately one-third of the families in the study live on farms; the remainder live in small towns. All of the families are white, and their annual income ranges from zero to $135,000, with a mean of $29,642. The educational level of participating fathers ranges from 8 to 20 years, with a mean of 13.5 years; the educational level of the mothers ranges from 8 to 18 years, with a mean of 13.4 years. The fathers range in age from 31 to 68 years, with a median of 40 years; mothers' ages range from 29 to 53 years, with a median of 38 years. Since families of less than four are excluded from the sampling frame, the study families, on average, are larger than would be expected from a general population survey. Families range from 4 to 13 members, with an average of 4.9 members.

Analysis Plan

For purposes of hypothesis testing, parental behavior is divided into two dimensions: Supportive parenting and harsh discipline. Supportive parenting is defined as the extent to which parents take an interest in their children's activities, talk with them about their problems, and show love and encouragement. Harsh discipline is defined as the extent to which parents are highly coercive (e.g., yelling, threatening, hitting) in their approach to exercising discipline. In an effort to reduce the problem of inflated associations between constructs due to shared method variance, parent self-report, child report, and observational ratings are used to form composite measures of the parenting constructs.

INTRAVENOUS ANTIBIOTIC THERAPY IN CYSTIC FIBROSIS: HOME VERSUS HOSPITAL

GRANTEE Tulane University School of Medicine

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PROJECT NUMBER MCJ-220556

PROJECT PERIOD 05/01/87–10/31/90

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	301,586	377,434	475,272	denied	n/a
Requested	301,586	400,813	429,312	45,988	n/a

* Indirect included

SUMMARY

Statement of the Problem

Over the past 50 years, the average life expectancy for a person with cystic fibrosis (CF) has risen from under 5 years of age to 20–25 years of age, due largely to improvements in antimicrobial therapy, particularly the use of intravenous (IV) antibiotics. However, because of the chronic, progressive nature of their lung disease, these patients experience more frequent and longer hospitalizations as they get older.

The administration of intravenous antibiotics at home has become a popular alternative to hospitalization in the past decade. Results from preliminary studies have indicated that home intravenous antibiotic therapy (HIVAT) might reduce the need for hospitalization without compromising care. However, no prospective, randomized, controlled trials have been performed to establish the safety, efficacy, patient acceptance, and cost of this type of therapy.

Research Questions or Hypotheses

The purpose of this study is to compare both short-term (2 week) and long-term (1 year) effects of HIVAT with those of traditional hospital IV antibiotic therapy on patients with cystic fibrosis who are having an exacerbation of pulmonary disease. The effects of the two therapies on the study population are compared in five major areas: Efficacy, safety, acceptance by patients and parents, psychosocial effects on patients and parents, and cost.

Study Design and Methods

This study is a prospective, multicenter, randomized, controlled clinical trial. Study patients are identified at the beginning of an exacerbation of pulmonary disease and are screened for inclusion in the study by a physician and a nurse or social worker. If patients are found to be suitable and agree to participate, they are randomized to either hospital therapy or home therapy after a short period of hospitalization, and each patient is followed for 1 year after enrollment. Data are collected during the initial exacerbation, during each subsequent exacerbation, and at clinic visits 6 and 12 months after enrollment. At these times, each patient has a chest roentgenogram, a complete physical examination, and pulmonary function tests that include forced expiratory volume (FEV_1), forced vital capacity (FVC), and the maximum rate of catalysis ($Vmax_{50}$).

Patient acceptance of treatment is measured by questionnaires given to participants at the end of the first exacerbation and at the 12-month visit, and by determining the percentage of patients who completed their assigned treatment course in each group and the percentage of those having a second exacerbation who agree to stay in their assigned group for treatment.

Anxiety and self-concept in patients and caretakers are measured by the Piers-Harris Children's Self Concept Scale, the Tennessee Self Concept Scale, the State Trait Anxiety Inventory for Children, and the State-Trait Anxiety Inventory. Coping skills of the caretakers are measured by the Coping Health Inventory for Parents.

Costs compared in the study are limited to three areas: Hospital or home-care company charges, physician charges for hospital care, and personal out-of-pocket expenses incurred by the patient and family during periods of IV antibiotic therapy either in the hospital or at home.

All patients receive both an intravenous aminoglycoside (usually tobramycin) and an anti-pseudomonal penicillin or cephalosporin (usually ceftazidime) every 8 hours during a pulmonary exacerbation. For patients randomized to home therapy, a primary caretaker is identified and taught the techniques for storage, preparation, and administration of the antibiotics. The patient and family are put in touch with a home-care company that sends nurses to evaluate the patient every 4 days. Patients in home therapy are hospitalized for at least 3 days during the initial exacerbation and any subsequent exacerbations. Duration of treatment in both groups is for a minimum of 10 days.

Population Description and Sampling Plan

Twelve centers are participating in the study. In addition to Tulane University, the other centers are: Arkansas Children's Hospital, Little Rock, Arkansas; Children's Hospital of Los Angeles, California; Hahnemann University, Philadelphia, Pennsylvania; Louisiana State University School of Medicine, Shreveport, Louisiana; St. Francis Hospital and Medical Center, Hartford, Connecticut; University of Alabama at Birmingham, Alabama; University of Florida at Gainesville, Florida; University of Kentucky Medical School, Lexington, Kentucky; University of Nebraska Medical Center, Omaha, Nebraska; University of Rochester Medical Center, Rochester, New York; and University of Wisconsin, Madison, Wisconsin.

All study patients have cystic fibrosis, and at the time of admission to the study all were hospitalized with an exacerbation of pulmonary disease. Of 756 patients screened, 486 were potentially eligible; of these, 36 percent were excluded because of patient or family situations that precluded the safe administration of HIVAT. After inclusion and exclusion criteria were applied, 196 patients were eligible. Of these, 61 percent refused to participate and 39 percent (78 patients) were enrolled in the study. One patient agreed to participate and was randomized but then withdrew from the study. Thus, data have been collected on 77 patients.

Analysis Plan

Data from the first exacerbation are compared by means of multiple regression analysis, with change on treatment (home versus hospital random assignment) adjusting for other covariates. Data from the year of followup are compared by means of a repeated measures analysis of variance. Changes are compared between treatment groups by means of multiple linear regression of the logarithm of total changes on treatment, adjusting for center differences.

SMOKING CESSATION/RELAPSE PREVENTION IN LOW-INCOME MOTHERS

GRANTEE Johns Hopkins University

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PROJECT NUMBER MCJ-240562

PROJECT PERIOD 11/01/87–10/31/91

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	184,973	222,565	219,117	228,266	Denied
Requested	292,934	388,528	372,066	406,973	378,954

* Indirect included

SUMMARY

Statement of the Problem

Impoverished African-American women are a particularly vulnerable population for experiencing the harmful effects associated with smoking, yet they have received relatively little attention in smoking cessation research. Cigarette smoking is a known risk factor for diseases of the heart and lungs among women, and for African-American women the relative risk of death from heart disease and cancer is greater than for white women. African-American women in the childbearing years also have a greater prevalence of hypertension, which, when combined with cigarette smoking, produces a significant risk for heart disease. An opportune time to intervene with this population is during the childbearing year, when many women present for medical care and may be motivated by concern for their infants to consider smoking cessation. Intervention during this period is particularly important because it also addresses the public health problems of low birthweight and infant respiratory illness associated with maternal smoking during pregnancy and the first year of life.

While considerable epidemiologic evidence is available on the risk of smoking to women and their children, very little is known about how best to motivate the pregnant woman to stop smoking. Although a number of studies have reported on the effectiveness of smoking cessation interventions for pregnant women, most studies have found no significant change in smoking behavior and/or have had methodological flaws that seriously weakened interpretability of the results.

Moreover, no study of smoking cessation and pregnancy, to our knowledge, has developed or tested the effectiveness of relapse prevention interventions, nor has any study developed or tested postpartum interventions (e.g., to enhance the maintenance of cessation after the initial motivation of fetal protection has passed). This study addresses these neglected issues, using an experimental design with biochemical confirmations in a large cohort of low-income, pregnant women and new mothers followed until 6 months postpartum.

Research Questions or Hypotheses

The general research hypothesis of this study is that pregnant smokers exposed to multiple smoking cessation and relapse prevention interventions will exhibit greater levels of reduction and abstinence than those not exposed. The primary aims of this study are to: (1) Develop multicomponent smoking cessation/relapse prevention interventions suitable for use in health care settings that serve low-income, minority women during the childbearing year; and (2) determine the behavioral impact of the multicomponent interventions on smoking cessation, relapse, and reduction rates, both during and after pregnancy.

Study Design and Methods

The interventions are tested among 467 pregnant current smokers who are randomly assigned to receive either (1) a prenatal and postpartum intervention (intervention group), or (2) usual clinic procedures with no special intervention (control group). The interventions include individual counseling in the use of self-help materials and supportive reinforcement by clinicians. Self-report and biochemical confirmation using saliva cotinine levels are the two primary measurement techniques used in the study. Interviews are conducted at five points in time: First prenatal visit; third trimester visit; immediately postpartum; 3 months postpartum; and 6 months postpartum.

Population Description and Sampling Plan

Study subjects are selected from women attending the obstetric clinics of The Johns Hopkins Hospital in Baltimore, Maryland. Approximately 80 percent of the patients attending these clinics are low-income women on medical assistance; approximately 80 percent of the patients are black, and most of the remaining patients are white. This population can generally be expected to reflect the universe of women who receive obstetric care in university hospital outpatient clinics in inner-city, predominantly black communities.

Analysis Plan

Initial hypothesis testing employs chi-squared tests based on dichotomous (continuous and prevalence) smoking versus abstinence outcomes. The association between the smoking versus abstinence outcome and multivariate effects (e.g., age, family composition, and parity) is examined using logistic regression models. In addition, life table survival analysis is employed to study in more depth the differences in treatment effects, particularly the effects of treatment at specified time intervals. Life table survival analysis techniques permit identification of high-risk periods for relapse (when interventions may be particularly appropriate). Finally, longitudinal data techniques are used for smoking/nonsmoking pattern analysis. Regression models are used to identify differences in the characteristics of subgroups of subjects found to relapse at different high-risk periods.

HOME INTERVENTION FOR INFANTS WITH FAILURE TO THRIVE

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PROJECT NUMBER MCJ-240568

PROJECT PERIOD 04/01/88–03/31/93

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	126,047	126,473	151,906	143,433	134,264
Requested	177,389	187,855	125,413	187,855	125,413

* Indirect included

SUMMARY

Statement of the Problem

This study is designed to implement and test the effectiveness of home-based intervention in promoting growth and development among infants with nonorganic failure to thrive (NOFTT). It is a partnership between a university department of pediatrics and a community-based agency with expertise in providing early intervention to at-risk infants and toddlers.

Measurement of growth is a standard procedure throughout the world for assessing the well-being of infants and young children. Infants who fail to achieve adequate growth, based on national standards, are classified as having failure to thrive, and are at increased risk for subsequent growth, developmental, and emotional problems. Although organic problems can interfere with growth, the majority of children with failure to thrive have no major medical problems contributing to their poor growth, and therefore can be classified as having NOFTT. Distortions in family functioning and parent-infant interactions are thought to be important factors in causing and maintaining NOFTT. This study is conducted among a very high-risk group of children: Low-income, inner-city, primarily African-American children who were born healthy, but who have not grown according to expectations.

Research Questions or Hypotheses

The hypothesis is that children with NOFTT who are living with families who receive weekly home visits for 1 year will experience better growth and development than children living in families who do not receive the intervention. We hypothesize that the mechanisms contributing to changes in children's growth and development are family functioning and parent-infant interaction, which are targets of the intervention.

Study Design and Methods

This study uses a randomized clinical trial design. Families are assigned to the home intervention group or the control group, using a stratified randomization procedure (by age, gender, and race). Families in the intervention group receive weekly home visits from a home intervention specialist for 1 year. The home intervention is provided by a community-based agency, and university staff remain blinded to the intervention status of the families. The Growth and Nutrition Clinic, a pediatric subspecialty clinic, has been established at the University of Maryland to provide evaluations and followup for children with NOFTT.

The intervention being tested in this study is based on ecological theory, in which attention is directed to the parent, to the parent-infant relationship, to the parent's relationship with her family, and to the access and utilization of friends and community resources. The intervention was designed following a thorough review of the literature and is based on home intervention programs from the fields of social work, special education, pediatrics, nursing, and psychology. The Hawaii Early Learning Program serves as a general guideline for a range of developmentally appropriate activities for the home interventionist to use with the family.

The home interventionist attempts to visit the families weekly. The initial goal of the home intervention is to develop a trusting relationship with the primary caregiver. The home interventionist completes personal contact records following each contact or attempted contact. The personal contact records include information on the content and details of the visit as well as the home interventionist's ratings of the cleanliness of the home, quality of the parent-infant interaction, appropriateness of the mother, and receptivity and motivation of the mother.

Families in the intervention group are given a notebook with a picture of the baby, a calendar to record appointments, information on resources and child development, and compartments for personal keepsakes. The notebooks are meant to help with the primary caregiver's structure and organization.

All families (both intervention and control) follow the same evaluation protocol. The initial comprehensive evaluation includes two clinic visits and a home visit, and addresses both outcome variables (growth and development) and process variables (family functioning, parent-infant interaction, and parental stress and support).

Assessments are carried out in the following areas:

1. Anthropometrics.
2. Mental, motor, and language development: A psychologist administers the Bayley Scales of Infant Development and the Receptive-Expressive Emergent Language Scale.
3. Health status: A pediatrician evaluates the child, reviews the child's medical history, and draws blood for a series of laboratory investigations.
4. Nutritional status: A nutritionist administers a 24-hour diet recall and reviews the child's feeding history and reported feeding problems.

5. Psychosocial status: A social worker interviews the primary caregiver (usually the mother) regarding her family of origin and psychosocial history.
6. Videotaped feeding observation: Families are informed that their child will be videotaped having lunch (the Growth and Nutrition Clinic provides age-appropriate food and eating environment). Videotapes are coded to provide an assessment of parent-infant interaction.
7. Family functioning and parental stress and support: These are assessed through a series of standardized self-report measures.
8. Home environment and child-centered quality of the home: All families receive an initial home visit, and the Home Observation for Measurement of the Environment (HOME) is administered.

A subset of the evaluation protocol is repeated at 6-month intervals (i.e., at 6, 12, and 18 months after the initial evaluation). The subset includes outcome measures (growth and development) and process measures (parent-infant interaction, as measured by a videotaped interaction; and family functioning, parent stress, and parent support, as measured by standardized questionnaires).

After the family has completed the 18-month protocol, a final home visit is made, and the HOME is again administered. In addition, we administer a consumer satisfaction questionnaire and give the family a copy of their videotape, which contains four parent-infant interactions which were videotaped over the 18-month period. Families continue to receive followup, growth monitoring, and nutrition counseling as necessary.

Compliance can be a major concern in a longitudinal study. The following procedures are used to promote compliance:

1. Reminder cards are sent and telephone calls are made to the caregiver prior to each appointment.
2. Names and addresses of extended family members are recorded.
3. Permission is obtained to request addresses from the Department of Social Services.
4. Holiday and birthday cards are sent to the family.
5. Payments are made for evaluation visits.
6. Babysitting is provided during visits to the Growth and Nutrition Clinic.
7. A copy of the videotape of the primary caregiver and the child is given to the caregiver at the conclusion of the project.
8. A caring atmosphere is maintained by a friendly, considerate staff who take pride in providing individualized attention.

Population Description and Sampling Plan

The Growth and Nutrition Clinic takes place one-half day per week in the Pediatric Subspecialty Clinic at the University of Maryland Hospital. Children are recruited from the pediatric clinics associated with the University of Maryland as well as from community providers. Recruitment criteria for the children include:

1. Age less than 24 months;
2. Full-term birth (greater than 36 weeks);
3. Appropriate weight for gestational age at birth;
4. No congenital disorders or major handicapping conditions; and

5. Weight-for-age below the 5th percentile, or weight-for-height below the 10th percentile, based on National Center for Health Statistics charts.

The primary pediatric site of the University of Maryland is the Pediatric Ambulatory Center, which provides primary care to approximately 6,000 children ages 0–19 from the neighboring inner-city community. The majority of the families have low incomes (either they receive Medical Assistance or they have no insurance), and approximately 80 percent are African American. In a preliminary survey of medical charts of 2-year-old children, we determined that approximately 5 percent would have met our recruitment criteria. If there are 1,200 children under 24 months of age and a referral/acceptance rate of 80 percent, we estimate a recruitment period of 3–5 years is needed to recruit 150–200 children.

Analysis Plan

Initial hypothesis testing is conducted using repeated measures analysis of variance with growth or development over time as the dependent measure, and intervention status as the independent measure. Because we do not expect all families to accept the intervention or to benefit in the same way, we perform a series of subgroup analyses to determine the conditions associated with optimal growth and development. Multivariate regression analyses are used to examine associations between the intervening (process) variables and the outcome variables. Finally, structural equation modeling is used to examine the patterns of change as a function of intervention status.

STUDY OF PSYCHOSOCIAL FACTORS IN MATERNAL PHENYLKETONURIA

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PROJECT NUMBER	MCJ-250529
PROJECT PERIOD	11/01/85–10/31/91

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	123,300	denied	144,661	denied	164,310
Requested	102,043	114,269	121,324	549,544	211,950

* Indirect included

SUMMARY

Statement of the Problem

Newborn screening and early treatment for phenylketonuria (PKU), an inherited disorder of phenylalanine metabolism, have resulted in the prevention of mental retardation in thousands of children over the past 25 years. As a direct result of that success, however, women with PKU who at one time would not have married or borne children are now in a position to have families of their own. Since nearly all of these women have resumed a normal diet during childhood, their pregnancies are at high risk for the complications associated with phenylalanine teratogenicity.

In New England, there are approximately 250 women between the ages of 12 and 45 with PKU, and the majority of these women are not institutionalized. These women are at high risk for bearing children with birth defects unless they begin appropriate dietary therapy prior to conception and remain on this therapy throughout pregnancy. For women with classic PKU (the most severe and most common form), risks to the developing fetus include mental retardation, microcephaly, and congenital heart disease.

Despite these well-documented risks, most women present to PKU clinics after they have become pregnant, when damage to the fetus may already have occurred. Education alone regarding risks does not appear to ensure adherence to medical recommendations. When women initiate dietary therapy after they are pregnant, they often have difficulties tolerating the special formula and adhering to the strict regimen. This places the fetus at further risk from ongoing exposure to toxic maternal levels of phenylalanine. Unless the issue of maternal PKU is successfully resolved, it threatens to erase in one generation the gains made since newborn PKU screening was initiated.

This study does not seek to address specific racial or ethnic health issues. Because of genotype dispersion, people in New England who have PKU are primarily of northern European ancestry. However, findings regarding prevention of unplanned pregnancy and adherence to prenatal treatment recommendations may be helpful in dealing with similar issues in other high-risk populations. While PKU affects both females and males in approximately equal proportions, this study focuses on women with PKU because of the risks associated with childbearing for these women.

Research Questions or Hypotheses

This study examines the psychological factors that may underlie adherence or nonadherence to medical recommendations regarding the prevention of unplanned pregnancies and dietary treatment in women with PKU. The hypotheses are based on a model of the maternal PKU lifecycle which includes four stages of behavior:

Stage 1: Prevention of unplanned pregnancies;
Stage 2: Conscious reproductive decision making;
Stage 3: Initiation of dietary treatment; and
Stage 4: Continuation of dietary therapy throughout pregnancy.

The following questions are addressed: Does success at one stage predict success at other stages? How do women with PKU change over time? Are the psychosocial factors that predict adherence to medical recommendations unique to women with PKU, or do similar factors predict behavior among women with diabetes mellitus and women with no known medical problems?

Study Design and Methods

Subjects are interviewed annually in their homes or at their PKU or diabetes clinic. The 2-hour standardized interview is based on the stage in the lifecycle model that is currently appropriate to the subject's situation. Extra interviews are administered if a subject enters more than one stage during the year. In order to monitor changes in life situations, 6-month call-backs are made between each interview session. The interview protocols include questions regarding current demographic information; open-ended and Likert-scaled questions related to PKU, diabetes mellitus, and childbearing; and several questionnaires.

The dependent or outcome variables include behavioral measures and quality of life measures. According to the four-stage model, the behavioral goals related to women with PKU for each stage are as follows:

Stage 1: Use of effective birth control if sexually active;

Stage 2: Conscious reproductive decision making based on accurate perceptions of risk information;

Stage 3: Treatment initiation prior to conception for women with PKU and diabetes mellitus; and

Stage 4: Maintenance of metabolic control during pregnancy.

There are five general categories of independent variables, which are viewed as predictors of the outcome variables: (1) Background variables, including IQ, marital status, and social class; (2) knowledge about issues relevant to a particular stage of treatment; (3) personality characteristics and mental health status; (4) attitudes and beliefs, including motivations and values; and (5) social support for treatment behaviors.

Population Description and Sampling Plan

The study subjects are 70 women with PKU and 2 comparison groups, composed of 68 female acquaintances of the women with PKU and 69 diabetic women. Subjects are matched for age, education, and marital status. All subjects are between the ages of 16 and 30 and have at least a sixth-grade reading level. Women with severe mental retardation or known serious medical complications are excluded. Subjects are recruited from clinic lists, public health registries, and newborn screening records.

Analysis Plan

Three types of studies are carried out:

1. A descriptive study of young women with PKU which addresses how much these women know about their medical condition, how they behave socially, what their needs are, to what extent PKU has affected their attitudes and behaviors, and how similar they are to women with diabetes mellitus and to women without known risks related to childbearing;
2. A correlational study involving the measurement of intervention-related and background variables that might predict behaviors that are related to outcome in maternal PKU; and
3. A prospective, longitudinal study that addresses how women with PKU change over time, and whether behavior at one stage predicts behavior at another stage.

INFANTS OF DEPRESSED ADOLESCENT MOTHERS

GRANTEE Boston City Hospital

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PROJECT NUMBER MCJ-250559

PROJECT PERIOD 12/01/87–02/28/90

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	79,550	80,673	4,929	n/a	n/a
Requested	79,550	80,673	18,642	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

Childbirth during adolescence is a major concern to clinicians and public officials because these births are so often associated with increased developmental, social, and medical hazards for both the mother and child. Despite these hazards, few investigators have identified potential mechanisms that may explain why parenthood during adolescence has such adverse effects on infants.

Recently, the striking similarity in the developmental and behavioral outcomes of the infants of adolescent mothers and the infants of depressed mothers was described. Cognitive development among both sets of infants and the interactional styles of the mothers are similar.

Research Questions or Hypotheses

The purpose of this research is to determine the prevalence of depression among adolescent mothers and whether infants of depressed adolescent mothers have poorer outcomes than infants of nondepressed adolescent mothers.

Study Design and Methods

Adolescent mothers who meet the study's eligibility requirements are consecutively recruited as they register for prenatal care at Boston City Hospital. Mothers are requested to bring their infants to the 12-month interview so that these infants can undergo detailed anthropometric evaluation and testing, using the Bayley Scales of Infant Development and the Infant Behavior Record.

The mothers undergo a detailed semistructured interview at the time they register for prenatal care, within 72 hours following the birth of their infant, and at 6 and 12 months postpartum. Demographic data and information about depression, social support, life stresses, drug use, infant temperament, and the number of injuries and hospitalizations are solicited. In addition, the mothers furnish urine for assay of metabolites of marijuana and cocaine at all encounters.

Depression is measured using the Center for Epidemiologic Studies Depression Scale (CES-D). This 20-item Likert scale is scored between 0 and 60, with scores greater than 16 consistent with depression. The measure is considered both reliable and valid in the adolescent population. Because of the potentially high prevalence of depression in this group, depression is also coded as the top 25th percentile score at all encounters.

Population Description and Sampling Plan

Adolescent women who register for prenatal care at Boston City Hospital are eligible for this study if, at the time of delivery, they consent to be interviewed at 6 and 12 months postpartum, speak English or Spanish, and have no major mental illness, and if their infant is full-term and spent less than 24 hours in the newborn intensive care unit.

The study sample consists of 127 women enrolled at the time of the birth of their child; 97 women (76.4 percent) completed the 1-year postpartum interview and brought their child to that encounter for anthropometric and cognitive assessment. The mothers are predominantly young (90.4 percent are under age 18), poorly educated (19.1 percent completed high school or college), minority (73.4 percent black), and poor (76 percent have monthly income less than $1,000, and 56 percent are on Aid to Families with Dependent Children). All of the infants were full-term and well at the time of discharge from the hospital, with a mean birthweight of 3,159 grams (± 490) and Apgar scores at 5 minutes ranging between 7 and 10, with a mean of 8.8 and a median of 9.0.

The mothers who did not complete the study ($N = 30$) were similar to those who did, with regard to maternal age, ethnicity, income, marital status, and depression measured at both 6 and 12 months postpartum.

Analysis Plan

The prevalence of maternal depression among adolescents will be delineated. We define the severity of depression based upon the CES-D, assessed both at 6 and 12 months postpartum. This allows us to define changes in maternal depression over the course of the infant's first year of life.

The Bayley Scales of Infant Development scores are treated as continuous variables but, in addition, we test for differences in the percentage of infants of depressed and nondepressed mothers whose scores fall below 80. A similar analysis is conducted for the Infant Behavior Record. Depression is coded as: (1) Not depressed at either 6 or 12 months postpartum; (2) depressed at either 6 or 12 months postpartum; or (3) depressed at both 6 and 12 months postpartum.

PRECONCEPTIONAL VITAMIN USE AND NEURAL TUBE DEFECTS

GRANTEE Trustees of Boston University

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PROJECT NUMBER MCJ-250567

PROJECT PERIOD 03/01/88–02/28/92

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	283,800	306,659	336,812	249,900	n/a
Requested	336,143	337,370	363,072	278,736	n/a

* Indirect included

SUMMARY

Statement of the Problem

Birth defects resulting from abnormal development of the embryonic brain and spinal cord are among the most traumatic birth defects, to both families and society. Collectively known as neural tube defects (NTDs), they include anencephaly (absent brain and skull) and spina bifida (various degrees of involvement of the spinal cord [myelomeningocele] and/or the surrounding tissues [meningocele]).

NTDs are relatively common birth defects, affecting approximately 1.5 per 1,000 births. Perhaps more important than the absolute numbers of affected infants is the burden they create for society in general and for the health care delivery system in particular. While NTDs include some defects that are of relatively minor consequence, and some that are incompatible with life, the large proportion of NTDs present serious and persistent medical and functional disabilities.

The etiology for the large majority of NTDs is unknown, though it is widely believed that they are of multifactorial origin. Based on experiments in animals and observations in women who previously had an NTD-affected pregnancy, it has been suggested that women who supplement their diets with multivitamins before conception would reduce by at least 50 percent their risk of having another NTD-affected pregnancy. In addition, although the evidence regarding preconceptional vitamin supplementation concerns only recurrent NTDs, it is generally assumed that occurrent NTDs might also be reduced by such supplementation. However, the potential risks of a massive preconceptional vitamin supplementation effort among women of childbearing potential must be considered. Specifically, the risk of actually increasing birth defects cannot be ruled out.

This situation requires resolution as rapidly as possible. We believe the most rapid, efficient, and feasible approach is a case-control study specifically designed to examine the potential benefit of preconceptional vitamin supplementation with respect to NTDs and, secondarily, to examine some of the potential hazards of excessive supplementation.

Research Questions or Hypotheses

This study has two primary hypotheses:

1. Multivitamin supplementation in the month immediately preceding the last menstrual period (LMP) is associated with a 50 percent reduction in NTDs; and
2. Folate supplementation in the month immediately preceding the LMP is associated with a 50 percent reduction in NTDs.

A secondary hypothesis is that excessive supplementation with vitamins or minerals in the month preceding or including conception, or in the months following conception, increases the risk of selected birth defects. This hypothesis is deliberately stated in broad terms. We will examine the collected data to test the existing hypothesis that excessive vitamin A supplementation is associated with increased risks of craniofacial malformations, heart defects, and brain defects. In addition, we will systematically review categories of specific defects to identify new hypotheses regarding excessive supplementation and birth defects.

Study Design and Methods

This study follows the case-control approach in order to test the primary and secondary hypotheses. A common data set will be used for both hypotheses.

Study subjects (cases and controls) are recruited through an active surveillance network of hospitals and clinics in the metropolitan areas of Boston, Philadelphia, and Toronto. Cases and controls consist of malformed infants and fetuses, and include liveborn infants under 6 months of age, stillborn infants, and therapeutic abortions (TAbs).

For the primary hypotheses, cases are subjects with NTDs, and controls are subjects with other malformations. The distribution of defects in the control series will approximate that found in the general population. Since pregnancies complicated by fetal malformation may be terminated by therapeutic abortion, it is important that the case series include NTDs that are electively aborted (and, therefore, that the control series include other malformations from the same setting). Vitamin supplementation may be related to socioeconomic status and health behaviors, which are likely to be associated with both the opportunity for prenatal diagnosis and the decision to undergo a TAb. For these reasons, NTDs that have been electively aborted are included in the study sample, along with their respective controls.

For the secondary hypothesis, there are various case groups. To test the hypothesis that excess vitamin A intake is teratogenic, case series include subjects with specific craniofacial, heart, and brain defects. To consider possible effects of excessive supplementation with other vitamins and minerals, additional case series include craniosynostosis and aortic stenosis. In these comparisons, controls consist of malformed subjects (with appropriate exclusions) not included in the respective case series.

A malformed control series is used in an effort to reduce the likelihood of recall bias, assuming that the accuracy of exposure reporting by mothers of malformed infants is different from that by mothers of normal infants.

Because it is important that bias not be introduced in our selection of cases and controls, we identify and enroll all study subjects in an identical fashion. In addition, controls are ascertained from the same institutions as cases.

Information on exposure to vitamins and minerals is obtained by interviewing the mother. The nurse-interviewer in each study center sends an introductory letter to mothers of designated subjects, followed by a telephone call. Informed consent is obtained prior to the interview, which is conducted in the mother's home at a time convenient to her. Interviews are conducted at home because we believe this setting is more relaxed and less threatening; it also affords the nurse the opportunity to examine available medication bottles. Interviews are conducted 3–6 months after delivery. The questionnaire, which takes approximately 45 minutes to administer, includes data on vitamin and mineral supplementation as well as other factors which may be related to supplementation or to the risk of NTDs or other birth defects.

Population Description and Sampling Plan

All mothers of infants (or fetuses) with major birth defects identified within 6 months of age and residing within the catchment area are eligible for inclusion in the study with the following exceptions: Women who do not speak English and do not have a translator are excluded because our interviewers are English-speaking only; women who have given up the study child for adoption are excluded for social reasons; and women who have previously been interviewed for our Birth Defects Study are excluded to reduce the potential for information bias.

We estimate that the total sample will consist of the mothers of approximately 350 subjects with NTDs and 1,900 subjects with other major birth defects, and that the demographic characteristics of the sample will be as follows: 90 percent white, 5 percent black, and 5 percent other races; 10 percent 20 years of age or younger and 10 percent over 35 years of age; and 15 percent with less than a high school education and 30 percent with a college degree.

Analysis Plan

Frequency distributions and cross-tabulations by outcome of all variables are generated. Odds ratios and test-based 95 percent confidence intervals (alpha = .05, two-tailed) are calculated to test and estimate associations for the relevant exposure variables. Potential confounding effects of other factors are assessed in a univariate manner by the Mantel-Haenszel procedure; each adjusted odds ratio is compared to the crude estimate. Logistic regression, using the method of maximum likelihood, allows estimation of odds ratios and confidence intervals while adjusting for the joint effects of potential confounders. The multivariate regression model includes terms for known risk factors for the outcome, as well as those factors that alter the crude odds ratio when controlled in a univariate manner.

For all relationships observed, effect modification among subgroups of women is examined by using two approaches. First, separate logistic regression procedures are carried out for subpopulations of interest. Second, indicator terms are created which represent all combinations of independent variables for which interaction is of interest.

Trends in associations are examined by using the Mantel extension test and logistic regression modeling.

COORDINATED CARE AND CASE MANAGEMENT FOR CHILDREN WITH SPECIAL HEALTH NEEDS

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PROJECT NUMBER MCJ-250581

PROJECT PERIOD 11/01/88–10/31/91

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	169,950	215,880	175,064	n/a	n/a
Requested	249,846	248,679	223,698	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

Case management as a service has a long history in the social service arena. In recent years, it has extended into the area of health care, specifically into the health care of children with special health needs and their families. Furthermore, several forces, many representing increasing consumer involvement in program and policy development, have revised the concept, from the management of cases to the coordination of care. This study seeks to examine aspects of care coordination and case management for families whose children have special health needs, including issues of health service utilization, the functional status of the child, perceived and unmet needs of families, and the psychological status of the child and primary caregiver.

Despite the relatively long history of efforts in care coordination for children with special health needs and their families, there has been little previous study and little careful documentation of the process of care coordination. Yet, it is a service that has received increasing attention and support from policymakers, program directors, and families; the provision of coordinated care raises important questions about its efficacy, appropriate target groups, types of services to be provided, and areas that care coordinators should address. This study consists mainly of an examination of the natural experiment in implementing care coordination by State Title V agencies. States differ in their enrollment policies and programs of case management or care coordination, thus providing the opportunity to examine these differences and some of their effects.

Research Questions or Hypotheses

This study is designed to examine families' perceptions of the processes and results of care coordination as provided by Title V programs. Although we expect no significant differences in hospital, physician, emergency room, or other health care utilization by provision or type of care coordination, we hypothesize that certain types of care coordination or the availability of care coordination will diminish perceived unmet needs and will be associated with improved psychological functioning of the child and parent as well as increased satisfaction with health services in general.

Study Design and Methods

This study uses a cross-sectional design that compares processes and outcomes for families and children with special health needs in States that vary in the intensity or presence of case management or care coordination services provided by their Title V programs. In collaboration with six State Title V agencies (Florida, Illinois, Iowa, Massachusetts, North Carolina, and Rhode Island), 100–120 families of children with special health needs are sampled from each state (except for Rhode Island, where the sample is smaller). The extent and type of case management, as viewed by families, is assessed.

The main measures used in the survey, beyond collection of basic demographic and illness-related questions, include: Impact of Illness on Family; service needs and health needs (two measures of unmet needs); the Center of Epidemiological Studies Depression Scale (CES-D), measuring depressive symptoms of the primary caregiver; the Personal Adjustment and Role Skills scale and the Child Behavior Checklist, measuring psychological status of the child; the Functional Status-II-Revised, measuring functional status of the child; the Family Support Scale; and measures of satisfaction and health service utilization.

Controlling for important demographic and health condition variables, the study assesses the effect of case management on use of both regular and emergency health services, participation of the child in usual daily activities (including preschool or school), psychological status of the child and of the primary caregiver, and perceived and unmet needs of the family.

Population Description and Sampling Plan

Six States were selected for geographic diversity, urban and rural mix, and differences in approach to care coordination. Florida and Massachusetts offer broad-based case management programs, each with 500–1,000 enrollees, mainly severely ill children with significant social issues in their families. Iowa and Illinois offer case management services only to children who are eligible for State Medicaid waivers for home- and community-based services. Rhode Island, originally selected as a comparison State that did not provide case management, has changed policies and has begun to offer these services. Rhode Island therefore has children who are receiving case management from the Title V agency and children who are not receiving those services. Finally, North Carolina officially provides no case management, but instead has a broad network of Title V clinics that serve approximately 30,000 children.

The sample includes children ages 1–16 years in any of four broad representative health condition groups: Bronchopulmonary dysplasia, technology dependence, spina bifida, and other conditions with high health services utilization patterns.

Analysis Plan

The project received 562 usable responses from families in the 6 target States. Initial analyses include descriptions of patterns of utilization of services (medical, dental, hospital, emergency, nursing, and associated therapies), the psychological state of the primary caregiver, satisfaction, and unmet needs. The study tabulates caregivers' perceptions of whether they are receiving case management services and the type of agency providing these services, along with families' perceptions of the types of services they receive from Title V agencies. Univariate and multiple regression techniques are used to determine the relationship between the presence or absence of case management and types of care coordination services received and utilization, satisfaction, maternal mental health, and unmet needs. Similar techniques are used to determine predictors of the types of families that receive care coordination services.

EARLY INTERVENTION COLLABORATIVE STUDY: PRESCHOOL PHASE

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PROJECT NUMBER
MCJ-250583

PROJECT PERIOD
04/01/89–12/31/92

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	244,364	342,439	284,385	228,538	n/a
Requested	327,007	411,947	347,164	286,612	n/a

* Indirect included

SUMMARY

Statement of the Problem

This study is designed to address both theoretical and pragmatic concerns facing the field of early intervention (EI) for young children with developmental vulnerabilities and their families. On a theoretical level, the study examines important questions about continuities and discontinuities in the process of development, the range of variation and predictors of adaptation in children with disabilities and their families, and the stability of individual developmental differences throughout early childhood.

From the practical perspective of service delivery, the study provides a longitudinal data base to inform the process of matching individualized intervention strategies to the specific needs of service recipients. Finally, the study investigates the durability of program effects over time. These challenges are particularly important in view of the policies established under P.L. 99-457, which mandates development of individualized family service plans for all children deemed eligible for publicly supported early intervention services.

This ongoing longitudinal investigation builds on findings that emerged during the first phase of the study, and is designed to explore the stability and durability of subgroup differences related to both vulnerability and resilience over the entire early childhood period. The study findings will provide vital information to assist policymakers and service providers in determining the most equitable and beneficial distribution of limited program resources. Because the study sample is 88 percent Caucasian, analyses related to racial differences are not feasible. However, the socioeconomic diversity of the study sample provides an opportunity to assess differences related to social class without the confound of ethnic diversity.

Research Questions or Hypotheses

The overall goal of the study is to test empirically the extent to which specific child and family outcomes are predicted by relatively stable status attributes, and the degree to which the relations between these attributes and outcomes are mediated by characteristics of the family ecology that may be amenable to change through service interventions. The study hypotheses are designed to test specific effects of early intervention services on domains of the family ecology when these services cease (coinciding with the child's third birthday), and the influence of the family ecology on child and family outcomes at 5 years of age. Three major hypotheses are tested:

1. The child's mastery behaviors at age 5 will be predicted by the quality of the mother's interaction with her child at age 3. Maternal interaction at age 3 will, in turn, be predicted by the intensity of early intervention services provided to the child and family between program entry and termination.
2. The pattern and extent of child maladaptive behavior at age 5 will be predicted by the degree of cohesion in the family at age 3. Family cohesion at age 3 will, in turn, be predicted by the extent of the mother's support group participation during the family's enrollment in an early intervention program.
3. Family adaptation at age 5, defined by parenting stress and impacts on the family, will be predicted by the perceived helpfulness of maternal social support networks at age 3. Maternal social support at age 3 will, in turn, be predicted by the level of participation in parent support groups between program entry and termination of EI services.

Finally, a substudy will be conducted to assess the transition experiences of children and families as they move from early intervention service programs (provided by the Department of Public Health) to preschool programs (provided by the Department of Education).

Study Design and Methods

This study is a continuation of a nonexperimental, longitudinal investigation of the development of 3 groups of children with disabilities and their families who were enrolled in 29 early intervention programs in Massachusetts and New Hampshire between November 1985 and December 1987. Phase 1 of the study was designed to test hypotheses about the unique contributions of child and family characteristics and early intervention services to changes in child competence and family adaptation over the first year of EI program participation. Phase 2, the current investigation, is designed to study the durability and stability of these effects and to test hypotheses regarding predictors and mediators of ongoing child and family development through the preschool years.

During the first phase of the study, each child and family was evaluated at home within 1 month of enrolling in EI (T1), and again after 1 year of intervention services (T2). The research design for the preschool phase includes four data points: In-home child and family assessments at the time of the child's third birthday (T3); collection of information from classroom teachers 6 weeks after the child's preschool entry (T4); and in-home child and family assessments (T5) and teacher reports (T6) at age 5.

The research design involves three critical elements: (1) Inclusion of three groups of children who have different patterns or types of developmental delay or disability; (2) repeated measurement of multiple dimensions of child and family development, using both traditional and innovative techniques; and (3) inclusion of accurate information on the quantity and type of services received by the study sample.

The protocol for each data collection point includes a core battery of child and family assessments in conjunction with information relevant to the specific data point (e.g., at T4, we examine parent perceptions of the transition process experienced from EI into preschool). The core battery for the child includes assessments at T1, T2, T3, and T5 of adaptive/functional skills, cognitive development, and spontaneous play behaviors.

Assessment of the child's mastery motivation behaviors begins with the T2 protocol and subsequently is included as a core dimension. For the family, the core dimensions include parenting stress, effects of the disabled child on family life, and social support (all assessed at T1, T2, T3, and T5), and mother-child interaction (assessed at T1, T2, and T3). Data are collected by project staff who remain independent of the service delivery system, and are blind to the study's hypotheses and to data collected at prior time points.

The research design does not include a nonintervention control group for three primary reasons. First, since all children with disabilities or delays are eligible for enrollment in EI programs and are entitled to preschool services, nonparticipating children and families are likely to differ from participating families in important characteristics, thus yielding problematic selection effects. Second, it would be virtually impossible and ethically untenable to retain a control group without services over the first 5 years of life. Third, the study's purpose is to identify the predictors and stability of individual differences in child and family development over the early childhood period, rather than to measure differences between those who do and do not receive services.

Population Description and Sampling Plan

The study sample includes 190 children with disabilities and their families who were recruited from 29 community-based early intervention programs in Massachusetts and New Hampshire at the time of referral for service. Eligibility was determined by the child's presenting developmental problem, as defined by each of 3 groups: Children with Down syndrome ($N = 54$); children with motor impairment, defined by abnormality in muscle tone with delayed or atypical motor development ($N = 77$); and children with developmental delays of uncertain etiology ($N = 59$).

The ethnic composition of the sample is 88.8 percent white, 4.7 percent Latino, 2.3 percent black, and 4.2 percent mixed racial or other ethnic origin. Fifty-six percent of the children are male. Despite their racial homogeneity, sample families reflect a fair degree of socioeconomic diversity. The mean education level for both mothers and fathers is 13.8 years. Nine percent of the mothers did not complete high school; 14 percent had more than 4 years of college. At time of study entry, the median family income was between $20,000 and $25,000 per year. Nineteen percent of the sample had an annual income of less than $10,000, while 36 percent earned more than $30,000 per year. The demographic characteristics of the study sample mirror those of the early intervention population in Massachusetts and New Hampshire.

Analysis Plan

Measurement of change in longitudinal data sets is one of the most difficult statistical challenges for those who study children and families over multiple data collection points. The primary analysis methods used in this study include analysis of variance and multivariate analysis of variance with and without repeated measures, multiple regression analysis (including stepwise and hierarchical methods and other variants such as LOGIT and TOBIT, depending upon the distributions of the dependent variables), and structural equation modeling.

In addition, recent advances in the use of hierarchical linear modeling as a technique for studying growth curves will be pursued to take full advantage of the multiple data collection points available for the full array of study outcomes.

IMPROVING MEMORY IN EMR CHILDREN

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PROJECT NUMBER	MCJ-260554
PROJECT PERIOD	07/01/87–12/31/89

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	85,095	89,429	34,090	n/a	n/a
Requested	127,957	134,646	33,689	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

This study assesses the effectiveness of a variety of instructional techniques designed to facilitate the performance memory of inner-city preschoolers and school-age retarded children across time and situation. Once identified, successful techniques will have wide applicability as teaching tools in the classroom, in intervention programs or demonstrations provided by early childhood specialists and educators. and in improved parent-child interactions. Although the primary purpose of the study does not address issues related to gender or race, the relevance of these factors for memory intervention might possibly be explored through some secondary analyses of the data.

Evidence suggests that facilitation of cognitive functioning may permit more normal levels of functioning in society for those who already suffer cognitive deficits or delays and for those who are at risk for developing learning problems. For instance, educable mentally retarded (EMR) children are at high risk for failing to achieve independent levels of maintenance in the culture. Improving cognitive functioning in areas such as memory may be one of the crucial factors in assisting an EMR child to achieve a more normal and independent level of functioning as an adult. In addition, determining whether these techniques are effective for urban preschoolers who are at greater risk for cognitive delays, and assigning these children to special education classes may reduce the need to intervene later.

The relation between memory-based interactions and children's memory skills is potentially important for understanding cognitive functioning in EMR children because there is evidence that these children receive less stimulation from the environment than normal children. This low rate of stimulation may, in some cases, cause the observed deficits and, in others, may amplify problems that already exist. Introducing memory demands more frequently than typically encountered may improve the children's ability to remember.

Research Questions or Hypotheses

This project examines the applicability of Vygotsky's model of cognitive development to memory instruction for inner-city preschoolers and older school-age mentally retarded children. In this model, the expert (usually an adult) guides the behaviors of the child novice in a joint activity, directing decisions concerning tasks that the child performs. More and more of the decision making is shared between the adult and child over time, until eventually the child regulates the activity in the task. Within this approach, then, shared activities that promote decision making and allow the child to accomplish task goals are viewed as central to promoting development. This study is being undertaken both to advance instructional techniques devoted to memory enhancement and to further theoretical specification of the processes involved in learning and memory.

This study addresses five central research questions:

1. Does an increase in memory demands, either alone or in combination with scaffolded prompts, lead to memory improvement?
2. Does guidance during recall lead to more improvement than demands alone?
3. Does strategy instruction, either alone or in combination with scaffolded prompts, lead to a greater increase in memory improvement than providing children a context to develop their own strategies without instruction?
4. If improvement occurs, how generalizable are the effects? Does transfer occur more in the presence of strategy instruction and prompting?
5. Do children who learn more of the training interaction and execute it more independently show greater improvement?

Study Design and Methods

To identify and develop effective memory-enhancing techniques, 106 average-ability preschoolers and 99 school-age EMR children participate in this study. Children in these two groups are randomly assigned to one of six memory-interaction conditions or to the control condition, with the restriction that assignment of experimenters and schools be approximately equal across conditions. The children work with an experimenter generally twice a week for 20 minutes each time, over a period of 2–3 months. During training, children interact with one of nine female experimenters who are matched by race to the child for all but 10 percent of the children. Both the pretest and the posttest are conducted by the same tester (who differs from the experimenter who trains the child).

In all conditions, children participate in six playful activities, such as coloring pictures or playing with blocks. In four of the conditions, children are then asked to recall certain aspects of the activities. The extent to which the experimenter provides explicit strategy instruction and scaffolding (i.e., assistance in helping children recall) is varied across these four conditions. In two of the conditions, children receive explicit instructions concerning the best way to recall (strategy instructions); in the other two, no strategy information is given (no strategy instructions). Within each strategy condition, the amount of scaffolding is varied. Children either receive prompts to aid recall or they do not receive prompts. At completion of training, children's ability to reenact the experimenter's memory or play routine is tested.

Before and after training, a wide variety of children's memory skills are assessed to determine how much improvement occurs across conditions. These tests include free and cued recall tasks, paired-associate tasks, a scene memory task, and an event recall task. Also, children's intelligence is assessed using the Stanford-Binet Intelligence Scale.

Population Description and Sampling Plan

Study subjects are average-ability preschool children ages 4–5 years and retarded elementary-school-age children in an urban setting. These two groups were selected because their intentional memory skills are poorly developed; they are at risk for developing, or have already developed, learning problems; and they need assistance in making the transition between use of involuntary and voluntary (intentional) memory skills. Because these children's skills are in the process of changing, they are perhaps more susceptible to the effects of instruction (particularly when embedded within less-structured play settings) than older or less delayed children. This permits a better test of theoretical models of memory processing, the effectiveness of intervention, and specification of those instructional components most successful in promoting development.

The average age of the preschool children is 4 years 5 months, with a mean mental age of 4.0 years. The average age of the retarded children is 8 years 5 months, with a mean mental age of 4.5 years. The children's mental ages are equivalent across conditions for both preschoolers and EMR children, *F*'s ≤ 1. An approximately equal number of girls and boys participate in each group. Among the preschoolers, there are 54 girls and 52 boys; among the EMR children, there are 44 girls and 55 boys. Among the preschoolers, 78 are black, 26 are white, and 2 are Asian; among the EMR children, 91 are black and 8 are white.

An additional 26 preschoolers and 13 EMR children initially participated, but were eliminated from the study because they moved, their attendance was erratic, they were removed from school by their parents, their parents no longer wished them to participate, they refused to cooperate, or because of experimenter error (incorrect training or pretest procedures). Finally, 29 preschoolers and 14 EMR children were not selected for the study due to high scores on the pretest.

The EMR children were recruited from 18 schools located throughout the Detroit Public School system. Children in this group met three criteria: (1) Identification by the local school district as EMR and in need of special education services within that category; (2) chronological age between 7 and 11 years; and (3) approval from parents and classroom teachers to participate in the study. Children with autism, Down syndrome, speech impediments, or under medication ($N = 5$) were excluded from the study.

Preschool children were recruited from 13 day care centers (12 located within the city and 1 in a suburban area). Children in this group were: (1) Ineligible for any special education services as determined by the local school district; (2) between 4 and 6 years of age; and (3) approved by their parents and classroom teachers to participate in the study.

Analysis Plan

Three sets of analyses are performed:

First, all posttest recall measures are analyzed in a series of 2 (Group: Preschoolers, EMR) × 2 (Strategy instruction: Strategy, No Strategy) × 3 (Memory demands: Demand-Prompt, Demand Only, Play) × 2 (Gender: Male, Female) analyses of covariance (ANCOVA), with pretest scores as the covariate. It is not possible to use multivariate analyses because the covariates vary across the multiple dependent measures. Followup ANCOVA analyses are carried out as appropriate. These analyses allow us to identify those aspects of training that lead to memory improvement, and are used to answer research questions 1–4.

Second, correlations are calculated between the posttest recall measures and the task used to assess children's memory of the training techniques.

Third, regression analyses are carried out to predict the posttest recall measures from mental age, pretest performance, and training memory performance. These analyses are used to answer research question 5.

OUTCOME EVALUATION OF A PEDIATRIC HEALTH CARE MODEL

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PROJECT NUMBER MCJ-360539

PROJECT PERIOD 01/01/87–12/31/90

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	154,553	190,357	277,441	Denied	n/a
Requested	155,415	202,770	167,018	61,202	n/a

* Indirect included

SUMMARY

Statement of the Problem

Research has identified a number of risk factors for preventable mortality and morbidity among children. Among these risk factors are medical conditions such as low birthweight, social conditions such as adolescent parenthood, and economic conditions such as poverty. Since these risk factors entail multidimensional problems, they are collectively referred to as "sociomedical risk factors."

Health policymakers are interested in attempts to reduce preventable mortality and morbidity among children who have one or more sociomedical risk factors. The traditional way to address these problems among high-risk children is through provision of health care. Delivery of health care to children from low-income families usually occurs in a number of settings, with limited kinds of care available at each site (e.g., the use of public health clinics for well-baby care and the use of clinics in hospital outpatient departments or emergency rooms for episodic illnesses). This system has been widely criticized as being fragmented and of poor quality as well as wasteful, in terms of both medical resources and parental time.

Recently, a model has been designed in New York City for organizing and delivering health care in a way that reaches children at high risk for preventable mortality and morbidity. This Pediatric Resource Center (PRC) Model is built upon the approach to care that was utilized in the Children and Youth Projects funded under Title V of the Social Security Act. The purpose of this evaluation study is to test this model of pediatric health care.

The Pediatric Resource Center Model provides comprehensive health care services for children in a team setting, maintaining continuity of providers and linkages to a network of health and social services, primarily for referral for services not available onsite. The model has four distinct components:

1. Availability of services (24-hour telephone access to a nurse or physician for consultation for emergency care);
2. Comprehensiveness of services (availability of nonmedical services such as nutrition, dental care, and social services);
3. Continuity of care (constancy of the primary care provider over time); and
4. Coordination (responsibility of one health care team for referral to specialty services and coordination of a treatment plan).

Despite the support in the literature for such a model of pediatric health care, this type of model has seldom been systematically evaluated in terms of child health outcomes. Most studies have assessed the quality of care provided, or focused on process measures and operational statistics. Very little is known about the relative effectiveness of this model.

Research Questions or Hypotheses

The study has two overall hypotheses: (1) The health of high-risk, poor children who are enrolled in a comprehensive pediatric care program will improve over time, compared to their health at entry into the program; and (2) the children enrolled in the model program will have better health outcomes than comparable children who have not been enrolled in such a program.

Study Design and Methods

This is a quasi-experimental study of equivalent groups: One group is comprised of children enrolled as patients in a pediatric resource center (the PRC group); the other group consists of children equally eligible for enrollment in a PRC but who are not enrolled, and who receive care from more generally available community sources (the comparison group).

Data are collected by structured interviews and medical examinations. Interviews usually are conducted with the child's mother, but occasionally a grandmother or guardian is interviewed instead. Interviews are conducted by specially trained bilingual (English and Spanish) interviewers. Medical examinations are conducted by onsite pediatricians who complete data collection forms specifically designed for the study. Data are collected at two points in time, approximately 1 year apart, for the PRC group, and at one point in time for the comparison group, matching the second point for the PRC children.

Almost 200 variables are utilized to assess outcomes in a variety of areas. These variables can be grouped into the following seven categories: Physical health, psychosocial health, functional health, preventive health behaviors, health knowledge and practices, utilization of health services, and unmet needs for care. Information for some variables is collected by both sociomedical interviews and pediatric examinations, which provide a validity check. For the most part, variables are assessed using measures developed and used in prior studies.

Population Description and Sampling Plan

This study focuses on the pediatric model as implemented at seven clinic sites in New York City. Each site is affiliated with a major hospital in one of the four largest of New York City's five counties. The PRCs serve children ages 0–19 whose families have incomes at or below 185 percent of the Federal poverty level (approximately $22,400 per year for a family of four). To be eligible for PRC services, children also must be at medical or social risk as defined by 12 sociomedical risk categories.

Among the children served by the PRCs, three high-risk groups were selected for inclusion in the evaluation study: Low birthweight children, children of adolescent parents, and adolescent mothers. PRC study participants reside in areas with the worst health and social indicators, and were new patients to the PRC at the time of enrollment into the study. Comparison children, matching the PRC group in essential characteristics (poverty status, risk category, area of residence), were drawn from birth certificate registries, child health clinics operated by the local health department, hospital nurseries, friends of participants, and late registrants (i.e., PRC registrants who had been eligible to enroll for at least a year, but had not done so). Children in the comparison group had never attended a PRC.

Almost 1,000 PRC participants were enrolled initially in the study. Of these, 622 were reinterviewed approximately 1 year later. A total of 575 comparison cases were enrolled in the study. All children were under 5 years of age, with most under age 3 at the time of enrollment in the study. Adolescent mothers ranged in age from 13 to 19 years. Child participants were divided equally between males and females. The adolescent group focused solely on the adolescent mother, and thus was comprised entirely of females.

The study population is diverse in its racial and ethnic composition. The study groups include Latinos (from Puerto Rico, the Dominican Republic, and other Latin American countries); African-Americans; and Haitian and other Caribbean (non-Hispanic) blacks. A small group of participants were designated as "other," including whites, Asians, and those of "mixed background" (e.g., Puerto Rican and African American).

Analysis Plan

The first analysis focuses on changes that occurred in the outcome variables in the PRC cohort between the initial assessment at the time of enrollment and the followup assessment approximately 1 year later. McNemar's test for dependent samples is utilized in addressing the first hypothesis.

The second analysis addresses the second hypothesis and comprises the main focus of the study. The two analytic groups used in this analysis (the PRC group and the comparison group) are assessed on several characteristics for comparability. Characteristics that are found to differ significantly ($p < .05$) between the analytic groups are used as covariates in all analyses.

Logistic regression is used to assess the impact of the PRC model. Each outcome variable is dichotomized at a logical cutpoint to simplify analysis. The regression equation includes any covariates identified as significantly different between the PRC and comparison groups.

DETERMINANTS OF ADVERSE OUTCOME AMONG TODDLERS OF ADOLESCENT MOTHERS

GRANTEE Research Foundation for Mental Hygiene, Inc.

INVESTIGATOR

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PROJECT NUMBER MCJ-360540

PROJECT PERIOD 11/01/86–10/31/91

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	101,527	179,648	190,002	195,047	153,925
Requested	130,970	208,921	220,548	195,047	187,544

* Indirect included

SUMMARY

Statement of the Problem

The importance of early prediction of poor mother-child outcome is clear. Identifying vulnerable groups early on, before the appearance of problems in child behavioral/developmental outcome, offers opportunity for prevention rather than amelioration. Moreover, problems in child behavioral/developmental outcome become increasingly stable after infancy.

Research Questions or Hypotheses

The overall objective of this project is to expand our understanding of the ways in which maternal psychosocial adaptation, expressed through the proximal childrearing environment, impacts upon developmental outcome in minority inner-city infants and children. The study tests the following hypotheses:

1. Developmental outcome in the child (as measured at 12, 24, and 36 months by cognitive ability, behavior problems, attachment, and observed interactive behaviors) will not be directly explained by maternal age. Maternal psychosocial attributes will contribute to child outcome, and their effects will be mediated by qualities of the proximal childrearing environment.
   a. Maternal depressive symptoms will be indirectly (and negatively) associated with child development at 12, 24, and 36 months through their impact on qualities of the proximal childrearing environment.
   b. Maternal childrearing attitudes will be indirectly associated with child development at 12, 24, and 36 months through their impact on the quality of the proximal home environment.

2. The quality of the extended family environment (as measured by child care arrangements, the alternate caregiver's psychosocial attributes, availability of childrearing and emotional support) will be associated with child development at 12, 24, and 36 months, both directly and indirectly through its impact on maternal psychosocial attributes.
   a. A positive extended family environment will act to compensate for the effects of adverse maternal psychosocial attributes on child development.
   b. A negative extended family environment will exacerbate the effects of adverse maternal psychosocial attributes on child development.
3. Where maternal depressive symptoms are substantial, the following maternal and child profiles will appear:
   a. The depressed mother, in interaction with her child, will show little positive affect and lack of responsivity to child cues, will ignore the child, and will be nonverbal. She will initiate few interactions, or will initiate them in a noncontingent fashion, intruding upon and distracting the child from play.
   b. The child will be insecurely attached and anxious, will show negative affect with mother and strangers, and will ignore or resist interaction.
   c. Child play will be primitive (e.g., mouthing), with low levels of functional play at early ages and of representational play at later ages. Cognitive/language scores on standardized tests will be compromised due to poor verbal abilities and inability to problem solve. Child Behavior Checklist scores will be elevated.

Study Design and Methods

Each eligible mother is approached within 48 hours of delivery, and asked to participate in a study of early parenting. Consenting mothers are interviewed in their hospital rooms by a bilingual interviewer, in their preferred language, English or Spanish. (Before beginning the study, all instruments were translated from English into Spanish and back-translated by a second individual to ensure the accuracy of the translation.) Questions are read aloud to all mothers and response option cards (in English and in Spanish) are used to facilitate responses. Mothers are interviewed regarding academic and employment history, living arrangements, social support, childrearing attitudes, and depressive symptoms.

Around the time of the child's first and second birthdays, families are assessed in the home and laboratory. Updated demographic information is obtained; social support, depressive symptoms, and childrearing attitudes are reassessed; information is requested on the allocation of household and child care responsibilities; and the quality of the home environment is measured, as is infant developmental status and (at 2-year followup only) mother's report of child behavior problems.

Information on living arrangements and demographics, including maternal age, education, and occupation, is obtained from each subject. Occupational status is assessed using a revised version of Duncan's Socioeconomic Index based on 1980 census figures. During followup assessments at 12 and 24 months, participants are asked who currently resides in the household, and whether there is another significant alternate caregiver for the child.

Childrearing attitudes are assessed using two subscales (strictness and aggravation) of the Parental Attitudes toward Childrearing Questionnaire, which presumably have negative implications for child development.

Social support encompasses a range of domains, including those of particular relevance to mothers of young children, such as child care assistance. Because our sample includes families in a variety of living arrangements, we ask about who provides support in each of these domains, in order to examine the relative contributions of various individuals. Traditional aspects of social support are assessed by three subscales of the Inventory of Socially Supportive Behaviors. The Division of Household Responsibilities and Childcare Scale is used to assess the mothers' reports of their own contributions and those of various relatives and friends to 15 routine household and child care tasks.

Depressive symptoms in mothers are measured using the Center for Epidemiologic Studies Depression Scale, and the quality of the home environment is measured by the Home Observation for Measurement of the Environment scale, administered in the course of a home visit. Developmental status is measured by the Mental Development Index of the Bayley Scales of Infant Development, which is administered by bilingual examiners at the 12- and 24-month followup assessments. Child behavior problems are assessed by mothers' report on the Child Behavior Checklist.

Population Description and Sampling Plan

Beginning in January 1987, a sequential sample of women giving birth on the service ward of a large inner-city hospital during a 12-month period was invited to participate in the present study. The population served by the hospital ward reflects the surrounding community, which is primarily African American and Hispanic, and predominantly low-income.

Exclusionary criteria include various perinatal conditions with potential impact upon subsequent maternal adjustment or child development. Infants with the following characteristics are excluded: Birthweight less than 2,400 grams, gestational age less than 35 weeks, or Apgar score less than 7. Infants who are part of a multiple gestation or who are affected by congenital anomalies or maternal drug abuse also are excluded. Inclusionary criteria for birthweight and gestational age are less stringent than conventional definitions of low birthweight and prematurity, permitting a greater range of infant outcomes while excluding truly high-risk neonates.

Adolescent mothers were sampled by a randomized block procedure to permit investigation of the effects of young maternal age on the outcomes of interest and to increase the variability in family structural types. The final sample includes 144 adolescents (less than 19 years of age) and 139 adults (more than 19 years of age). Of the 283 subjects in the original cohort, 181 (65 percent) received complete 12-month assessments and 153 (55 percent) received 24-month assessments. Subject loss was largely explained by families who had moved, reflecting the high mobility of the sample. Based on *t* tests and chi-square analyses, comparing retrieved and lost cases, there is no evidence of selective dropout at either 12 or 24 months on the basis of maternal age, country of origin, ethnicity, education, language spoken, receipt of public assistance, parity, social class, or paternal age or education. Nor do the retrieved and lost subjects differ in measures of postnatal support, depressive symptoms, or childrearing attitudes.

Analysis Plan

Analysis begins with examination of frequency distributions and measures of central tendency and variation in all continuous variables. Next, to reduce the total number of variables, we combine a number of significantly intercorrelated variables into composites or sets of variables, when justified on the basis of statistically significant correlations, theoretical content, and the role they play in the logic of the research questions.

Having examined the univariate and bivariate distributions of variables, we explore relationships among independent variables and their impact on child outcome over time. Multiple regression/correlation analysis (or a generalization of this method) is used both because of its ability to represent information as a set of variables and its ability to partial out the effects of any factor (or set of factors) from the effects of any other research factors.

We proceed through the hypotheses in an orderly way, expanding the simplest explanation of outcome to encompass more complex models that better describe the relationships of multiple factors to outcome. A hierarchical regression procedure is used, with sequencing of variables determined a priori on the basis of the literature and our own previous work; R^2 and partial coefficients are determined as each variable joins the others.

The study posits that the frequently reported associations between young maternal age and adverse mother and child outcome will be largely explained by the associations between maternal age and selected psychosocial and environmental variables.

Hypothesis 1 describes the contribution of demographic, psychosocial, and environmental factors to child outcome. Our initial study has suggested the direction of effects and some relative effect sizes. Subhypotheses are confirmatory and are first tested individually. The significance of all partial effects is determined, including possible interaction terms. We anticipate high intercorrelations among maternal variables (depressive symptoms, childrearing attitudes), and significant associations with the dependent variable, enabling us to enter the psychosocial variables into the final equation as a composite. We then determine the significance of the change in R^2 as this factor joins the summary measure of proximal home environment. Next, possible interaction terms are entered as a set of variables. Finally, maternal age is entered to determine whether age accounts for additional independent variance in outcome, once maternal psychosocial factors and home environment are considered.

Hypothesis 2 posits that the extended family environment will affect child outcome, both directly and indirectly, through its maternal psychosocial attributes. We explore the nature and role of the extended childrearing environment to determine the direction(s) of effects and the components of that environment actually accounting for outcome variance. A multiple regression procedure is used to explore main and interaction effects of the predictors on child outcome. Although maternal age is not explicitly considered in the hypothesis, its inclusion (adolescent versus adult group) as a final step in the equation will tell us how much of the variance in outcome is still explained by maternal age, over and above the proportion accounted for by other independent variables.

Hypothesis 3 is strictly exploratory, since there is little empirical work relating maternal psychopathology and observed maternal interactive behaviors to specific child outcomes. Again, a regression approach evaluates direct and indirect effects of maternal depression on child outcome, and explores the mediating role of maternal interactive behavior. Subscales of measures are examined separately to take advantage of the richness of the observation measures, with less attention to the problem of Type I errors.

A MULTIDIMENSIONAL HEALTH STATUS INDEX FOR INFANTS

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PROJECT NUMBER	MCJ-360571				
PROJECT PERIOD	10/01/88–09/30/90				
COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	128,357	123,431	n/a	n/a	n/a
Requested	146,112	143,430	n/a	n/a	n/a
* Indirect included					

SUMMARY

Statement of the Problem

Humanistic, methodologic, and economic concerns require design and evaluation of child health services on the basis of events that are more common and less extreme than infant death. Although the infant mortality rate continues to be used as a health index for population groups, it no longer provides an adequately sensitive measure in western countries. Infant mortality is now sufficiently uncommon that differences can be detected only in relatively large population groups or over extended periods of time. Furthermore, infant death represents an extreme event in the continuum of health.

Research Questions or Hypotheses

The goals of this study are to: (1) Explicate several dimensions of infant health and its determinants in order to develop a model that will guide health service delivery in the first 2 years of life; (2) develop, under the guidance of that model, a readily usable, multidimensional health status index based on diagnoses recorded on encounter forms commonly used in community health centers and pediatric practices; and (3) validate the assumption that the different dimensions of this index reflect the influences of different determinants of child health, including genetic factors, health system functioning, parental behaviors, and physical and social attributes of the child's environment.

We anticipate that this index ultimately would be used as: (1) A means to guide health resource allocations to different regions and different population groups; (2) the dependent variable in evaluation studies testing health service interventions; (3) the dependent variable in epidemiologic studies attempting to identify determinants of health status differences; and (4) evidence in the efforts to shape social policy and programs beyond health services in a way that maximizes opportunities for children to attain their full developmental potential.

Study Design and Methods

A 16-member panel of community-based and academic general pediatricians rated 346 problems encountered in the primary care of infants. Each problem was rated on the following characteristics: (1) Severity of the problem; (2) impact of health services on its prevention; (3) impact of health services through treatment; (4) impact of biologic and genetic factors, parent behavior, social environment, and physical environment on the etiology of the problem; and (5) impact of risk factors in these same categories on the severity of the problem. The impact of risk factors and health services was rated on a four-point scale: (1) none/rarely, (2) slight/sometimes, (3) moderate/often, and (4) great/usually.

Mean impact ratings are used to determine membership of diagnoses within morbidity clusters. Diagnoses with a mean impact rating above a cutoff of 2.5 for risk factors in a certain category (e.g., parent behavior) are included in the cluster representing that category of risk factors.

Of particular interest are morbidity clusters that include diagnoses with similar ratings for impact of risk factors on etiology. The morbidity clusters based on etiology include biologic/genetic, parent behavior, social environment, physical environment, and medically preventable factors. The score for a particular morbidity cluster is the incidence rate for all diagnoses that are members of the cluster. The incidence of all diagnoses falling within a particular morbidity cluster might be reduced by a common approach to prevention. Within each cluster, separate scales are developed for chronic and acute problems. For the chronic problem scale, person-incidence rates are used: Each chronic problem is counted only once for a child, regardless of the number of occurrences for the child in the data base. For the acute problem scale, episode-incidence rates are used: Each occurrence of a problem (i.e., each new episode) increases the frequency count for the child.

Construct validation is essentially hypothesis testing. Hypotheses useful in validation of morbidity cluster scores assess their meaning. For the parent behavior morbidity cluster score, for example, we test the hypothesis that the score correlates with more direct measures of parents' health-related behaviors (e.g., maternal smoking). Direct measures are obtained through home visits and medical record abstractions. During home visits, instruments are administered in the following areas: Behavior (Child Behavior Checklist), home environment (Home Screening Questionnaire), and development (Denver Developmental Screening Test, Early Language Milestones). A health interview, similar to the National Health Interview Child Health Supplement, is also conducted.

From data obtained through these instruments, variables are derived that can be grouped on the basis of hypothetical relationships with morbidity cluster scores. Groups of 5–10 variables are identified that should have a higher correlation with one of the morbidity cluster scores than with others. For example, variables in the parent behavior group (maternal smoking, maternal education, maternal age, breastfeeding, Home Screening Questionnaire) should correlate with the parent behavior morbidity cluster score but not with the biologic/genetic morbidity cluster score. In addition to the creation of variables that can be grouped by risk factor category, the traditional infant health status indicators such as parental perception of health, hospitalization, and low birthweight are also derived from data. Most morbidity cluster scores should correlate with traditional health indicators; these correlations, unlike those for groups of risk factors, will not be cluster-specific.

Population Description and Sampling Plan

The morbidity cluster scoring technique is applied to morbidity histories of a birth cohort of 1,778 children from a wide range of socioeconomic backgrounds who were stable patients in 3 community pediatric practices in Rochester, New York. Practices include a health maintenance organization, a hospital-based primary care center, and a community health center. Study participants met the following inclusion criteria: (1) Birth between January 1, 1987 and October 31, 1988; and (2) visits before 4 months and after 15 months of age. Encounter form data, collected through October 1990, is analyzed for the first 2 years of life. For purposes of validation, a 20 percent sample (349 children) was randomly selected from the study population to become a validation sample. For children in this sample, information about health status is obtained through home visits and medical records in addition to billing claims.

The 1,778 children made 32,412 visits (18.2 visits per child) during the first 2 years of life, and 35,085 diagnostic code (International Classification of Diseases [ICD]-9) entries were made at these visits (1.08 per visit). Of the 35,085 code entries, 3,931 represented codes that were invalid or did not specify morbidity (e.g., the code itself means followup), and 11,538 entries indicated well-child care. Of the remaining 18,896 valid ICD code entries, only 720 (3.8 percent) signified codes that had not been presented to expert panel members for rating. The 349 children in the validation sample made 6,746 visits (19.2 visits per child), and 7,430 diagnostic code entries were made at these visits (1.10 per visit).

Analysis Plan

Psychometric properties of expert panel ratings and morbidity cluster scores are assessed. On this basis, techniques for morbidity cluster scoring, outlined above, may be modified.

Construct validation focuses on convergent and divergent validity. Convergent relationships are those in which the morbidity cluster score and the validation variable represent closely related or even identical traits. A convergence index is defined as the proportion of expected convergent relationships that were observed. A discriminating pattern is one in which statistically significant correlation with the validation variable (such as the Child Behavior Checklist) is anticipated for one morbidity cluster score (such as parent behavior) but not for another (such as biologic/genetic).

For a discrimination index, the denominator is the number of pairs of validation variable–morbidity cluster score relationships for which a discriminating pattern was anticipated. The numerator is the number of pairs of validation variable-morbidity cluster score relationships for which a discriminating pattern was found. Evidence in support of construct validity is provided if the convergence or divergence indexes achieve values that are greater than those expected by chance alone.

STUDY OF HOME VISITATION FOR MOTHERS AND CHILDREN

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PROJECT NUMBER MCJ-360579

PROJECT PERIOD 09/30/88–08/31/93

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	324,379	450,486	465,178	305,865	16,109
Requested	324,379	453,486	465,178	305,065	16,109

* Indirect included. Jointly funded by the National Center for Nursing Research and the Maternal and Child Health Bureau.

SUMMARY

Statement of the Problem

In recent years, home visitation has been identified by the General Accounting Office as a promising early intervention strategy, and by the U.S. Advisory Board on Child Abuse and Neglect as the best-documented strategy for preventing child abuse and neglect. However, there have been no large-scale trials of home visitation for low-income families living in major urban areas. This study tests whether prenatal and postpartum nurse home visitation can improve a wide range of maternal and child health problems in women and children from low-income, inner-city families. The evaluation replicates a study carried out by the principal investigator several years ago in Elmira, New York.

Research Questions or Hypotheses

The overriding hypotheses of the larger study are that (1) the home visitation program will promote the health and well-being of the participating women and children, and (2) the effectiveness of the program will be greater for women and children who are at greater social, economic, or behavioral risk for the particular problem under consideration. In addition, we hypothesize that a financial investment in prenatal nurse home visitation eventually will be recovered by avoiding subsequent costs associated with maternal and child dysfunction.

We have conceptualized the trial as representing four separate studies, each directed toward testing the impact of the program on separate domains: (1) Outcomes of pregnancy, (2) maternal life-course development, (3) child health and development, and

(4) government expenditures. Within these four domains, we have specified detailed primary and secondary hypotheses.

With respect to outcomes of pregnancy, we hypothesize that the mean birthweight and length of gestation of infants born to mothers visited by nurses during pregnancy will be greater than that of newborns assigned to the comparison group. Secondarily, we hypothesize that the program will influence birth outcomes predominantly through improving women's health-related behaviors. Improvements in these behaviors have both direct effects on birthweight and length of gestation and indirect effects mediated by improved obstetrical health (e.g., rates of kidney infections, hypertensive disorders of pregnancy, and sexually transmitted diseases).

With respect to maternal life-course development, we hypothesize that nurse-visited women will attain greater educational achievement, will find employment more frequently, and eventually will depend on Aid to Families with Dependent Children less frequently than their counterparts in the comparison group.

With respect to child health and development, we hypothesize that nurse-visited children, compared to their counterparts in the comparison group, will have fewer incidents of child abuse and neglect, behavioral problems, and health care encounters for injuries and ingestions; shorter intervals of underimmunization; less iron deficiency; and more advanced cognitive development. We hypothesize that the program will influence child health and development through the nurses' efforts to promote the qualities of care that women and other family members provide to their children. Improvements in these qualities of caregiving have direct effects on children's health and development as well as indirect effects mediated by improvements in the physical environment in the home, such as safety and opportunities for intellectual development.

Finally, we hypothesize that the financial investment in prenatal nurse home-visitation services eventually will be recovered by avoiding subsequent costs associated with maternal and child dysfunction.

Study Design and Methods

We enrolled and randomly assigned 1,139 subjects to 1 of the 4 treatment conditions detailed below. The model on which we base randomization includes five classification factors that we expect to be important in our subsequent evaluations and in achieving equivalent samples across treatment groups. These factors are race, maternal chronological age, gestational age at enrollment, employment status of head of household, and geographic region of residence.

In Treatment Group 1, 166 families receive free round-trip transportation for scheduled prenatal care. This group does not receive any postpartum services or assessments. The purpose of this group is to increase the prenatal sample size for assessments of pregnancy outcomes.

In Treatment Group 2, 515 families receive free round-trip transportation for scheduled prenatal care, and developmental screening for the child at 6 months, 12 months, and 24 months of age.

In Treatment Group 3, 230 families receive free round-trip transportation for scheduled prenatal care, intensive nurse home visitation services during pregnancy, 1 postpartum visit in the hospital before discharge and 1 postpartum visit in the home, and developmental screening for the child at 6 months, 12 months, and 24 months of age.

In Treatment Group 4, 228 families receive free round-trip transportation for scheduled prenatal care, intensive nurse home visitation services during pregnancy and through the child's second birthday, and developmental screening for the child at 6 months, 12 months, and 24 months of age.

We determine the effectiveness of the prenatal home visitation service by comparing the health of the 458 women and newborns visited by nurses during the pregnancy (treatment groups 3 and 4) with 681 women and newborns assigned to receive comparison services (treatment groups 1 and 2). We test the effectiveness of the postnatal program by comparing 228 women and children visited during the first 2 years postpartum (treatment group 4) with 515 women and children assigned to comparison services (treatment group 2).

Research interviews are administered to all four treatment group subjects at intake, and at 28 and 36 weeks of pregnancy. In addition, we carry out abstractions of the obstetrical, labor, delivery, and newborn medical records for all subjects. During the postpartum phase of the study, treatment groups 2 and 4 complete research interviews when the child is 6, 12, and 24 months of age. We also conduct abstractions of the pediatric medical record and social service record for treatment groups 2 and 4.

Population Description and Sampling Plan

The population sampled for this study consists of low-income primiparas who reside in Memphis, Tennessee, who register in the study prior to the 29th week of pregnancy, and who meet no more than one of the following criteria: (1) High school graduate, (2) married, or (3) currently employed. We limited the sampling to those patients registering for care at the Regional Medical Center at Memphis because the vast majority of low-income patients in Memphis register for care at this center.

The profile of the sample is as follows: 92.4 percent are black; mean age at recruitment is 18.1 years; 2.7 percent are married; 31 percent have a high school diploma; mean number of years of education is 10.3; mean number of weeks gestation at recruitment is 16.5; 6.2 percent are employed; 55.3 percent of those who are the head of household are employed; and 85 percent live below the Federal poverty level.

During the prenatal phase of the study the attrition rate was no more than 10 percent from all causes, including miscarriages, stillbirths, and relocation. For the postnatal phase of the study, we expect no more than 25 percent attrition (total) by the time the child reaches 2 years of age.

Analysis Plan

In order to simplify our initial analyses of program effects, many dependent, intervening, and exogenous variables consist of scales summarized by factor analysis or according to a priori scales, either developed by us or adapted from other investigators.

The initial step in investigating program effectiveness is to examine the main effects of treatments upon dependent variables (e.g., child health and development outcomes). For the normally distributed variables, we use the general linear model; for dichotomous or low-frequency count data, we use logistic regression or log-linear models. Exogenous variables used in testing program effects are selected as follows: Correlations of dependent variables with exogenous variables are examined. Exogenous variables that either demonstrate significant correlations or are important on theoretical grounds are selected for possible inclusion as covariates in subsequent analyses. Attention is paid to the problem of multicolinearity. Where exogenous variables are highly correlated, they likely will be collapsed into a single summary variable.

A final set of covariates is derived through a set of analyses in which subsets of all the possible covariates are included in the model. Thus, for each dependent variable the model includes all factors specified in the classification structure, and a set of other exogenous variables entered as covariates.

In order to determine whether the effect of the intervention is stronger for hypothesized at-risk subgroups, two different analyses are performed, depending on whether the particular risk characteristic is quantitative or categorical. In cases where the risk characteristic is categorical, separate analyses of variance are conducted on each dependent variable, with treatments and the categorical exogenous variable (e.g., age [expressed as a categorical variable], head of household employed) included as classification factors. The main effect of the exogenous variable, along with the exogenous variable-by-treatment interactions, are thus brought under separate analytical examination.

In order to test the interaction of treatments with quantitative exogenous variables (e.g., age in years, degree of social support), the variable of interest is included in the model as a covariate and the homogeneity of regressions is tested across levels of treatment and other classification factors. Where regressions differ, we can infer that the experimental effects have varied as a function of some feature of the individual, the family, or the context in which they are functioning.

Two major sets of analyses are conducted using intervening variables. The first set is aimed at validating the treatment effects. In these analyses, intervening variables are analyzed as dependent variables.

As in the analyses of program outcomes, sets of exogenous variables for each intervening variable are identified either on theoretical grounds or by means of correlation screening, and the intervening variables are analyzed with these exogenous variables in the model. Significant differences among treatments on intervening variables can be interpreted as evidence for the effectiveness of the treatment strategies in altering facets of the environment that they were designed to affect.

Once the intervening or mediating variables that differentiate the treatment groups have been identified, we determine their theoretical relevance and analyze their relations with the dependent variable of interest. Those intervening variables that emerge as significant or that have theoretical importance are treated as covariates in subsequent analyses, along with previously identified exogenous variables. If a previously significant treatment difference on a particular outcome drops to nonsignificance with one or more intervening variables in the analysis as covariates, inferences about the processes set in motion by the program can be drawn.

It should be noted that the use of covariance for this purpose is simplified if homogeneity of regressions exists between intervening and dependent variables across levels of treatment. This requirement will be tested. The discovery of nonhomogeneous regressions would indicate that interactions exist between the intervening variables and treatments. If such interactions exist, they will then become the focus of the analysis and interpretation of results.

MATERNAL SMOKING AND VITAMIN/ANTIOXIDANT STATUS

GRANTEE Our Lady of Mercy Medical Center

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PROJECT NUMBER MCJ-360582

PROJECT PERIOD 06/01/89–05/31/92

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	41,743	70,177	42,320	n/a	n/a
Requested	48,695	47,007	20,345	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

Cigarette smoking during pregnancy is dangerous for the mother, the developing fetus, and the newborn infant. After birth, infants and young children of parents who smoke cigarettes also risk ill health due to passive or involuntary exposure to cigarette smoke in the home. However, little is known about the mechanism(s) by which cigarette smoking increases morbidity in these groups. Our preliminary studies indicate that pregnant women who smoke and their infants have low-to-deficient levels of two nutrients (vitamins C and E) despite daily intakes of both nutrients at levels equal to or greater than the current Recommended Dietary Allowance (RDA).

Vitamin C and vitamin E, as required nutrients, are necessary for normal maternal and fetal/infant health during pregnancy and lactation. Both vitamins also are endogenous antioxidants that can detoxify free radicals and other oxidants present in or generated by cigarette smoke. As such, vitamins C and E in adequate endogenous levels may have additional (nonvitamin) roles during pregnancy and lactation and may decrease both the severity and incidence of morbidity found in infants of mothers who smoke cigarettes. Our preliminary findings are, therefore, significant and relevant to several of the research priorities set forth by the Maternal and Child Health Research Grants Program.

Addressing racial or ethnic health issues is not a primary aim of this research. However, because the population in this study is approximately one-third black, one-third Hispanic, and one-third white, issues such as cigarette use by pregnant women, exposure of infants to cigarette smoke, and dietary intakes of required vitamins are explored during our secondary analysis of the data collected in this study.

Research Questions or Hypotheses

Because cigarette smoking during pregnancy/lactation is dangerous to the mother, the fetus, and the newborn, every effort must be made to prevent tobacco use during pregnancy and lactation. An additional goal must be to provide for the health and nutritional needs of women who are unable to stop their cigarette use during pregnancy and lactation. Our preliminary findings indicate that the current National Research Council/National Academy of Sciences RDA for vitamins C and E fails to maintain acceptable status for these vitamins in cigarette-smoking pregnant women and their newborn infants. This research examines whether different dietary levels of vitamins C and E (supplementation above current RDA levels) improve the vitamin C and vitamin E status of cigarette-smoking women during pregnancy and lactation and whether this improvement in maternal status directly affects the vitamin C and vitamin E status of newborn and nursing infants.

Study Design and Methods

This research uses a quasi-experimental clinical control trial study design. The study will be observational in nature (i.e., women who volunteer to participate cannot be randomly assigned to either smoking or nonsmoking groups). Care is taken to collect additional data from all study subjects in order to control for confounding factors reported to be associated with cigarette use, such as use of alcohol, drug use, poor eating habits, and education.

This study is experimental in design in that we will determine whether an intervention procedure (vitamin C and vitamin E supplementation) affects the maternal/infant outcome that was observed in our pilot study. The study is also double-blind in relation to the vitamin/placebo preparations to be administered to all study subjects.

Healthy, well-nourished pregnant women are recruited to participate in the study. Each woman's dietary and smoking habits (for both smokers and nonsmokers) is defined both by answers to a standardized questionnaire and by measurements of serum vitamin C, vitamin E, and nicotine and cotinine levels in an initial blood sample obtained at the first prenatal clinic visit. Women are asked to volunteer for the study, based on their age, parity, and gravidity data, and on information obtained from the initial questionnaire and biochemical testing. A total of 130 women are recruited and divided into smoking and nonsmoking groups. Study volunteers are recruited during their first trimester of pregnancy and will remain in the study for approximately 13 months. Infants of study volunteers are enrolled into the study at birth and remain in the study until they have completed their 6-month (well-baby) clinic visit. All volunteers are provided with a prescribed prenatal vitamin/mineral preparation (Stuart-Prenatals) free of charge. In addition, the six study groups are supplemented as follows:

Group 1: Nonsmoker controls, who are not given additional vitamin or placebo preparation ($N = 30$);

Group 2: Nonsmokers who are given supplementation with placebo ($N = 20$);

Group 3: Smokers who are treated with placebo ($N = 20$);

Group 4: Smokers who are given 30 mg of vitamin C plus 15 I.U. vitamin E as an additional supplement ($N = 20$);

Group 5: Smokers who are given 60 mg of vitamin C plus 15 I.U. vitamin E as an additional supplement ($N = 20$); and

Group 6: Smokers who are given 120 mg of vitamin C plus 60 I.U. vitamin E as an additional supplement ($N = 20$).

All study subjects, except those in group 1, take one supplemental capsule preparation each day of the study. On three occasions during pregnancy (during the first, second, and third trimester), the subjects complete a detailed dietary and smoking habit questionnaire. On these three occasions, each woman provides a venous blood sample for biochemical analysis. Immediately prior to birth or at birth, additional samples of maternal venous blood, cord blood, and placental tissue are obtained for biochemical analysis. In addition, information is obtained on the outcome of pregnancy (gestational age, birthweight, height, Apgar scores), including any complications.

After birth, an initial blood sample is collected from all study infants prior to initiation of feeding (4–8 hours after birth). A second neonatal blood sample is collected immediately prior to hospital discharge (between days 2 and 4). In addition, a maternal colostrum sample is collected whenever possible. On five additional occasions (at 2 and 4 weeks, and at 2, 4, and 6 months), all the women are scheduled into a well-baby clinic. On each occasion, a maternal blood sample and an infant blood sample are collected for biochemical testing.

A total of more than 5,000 biological samples are collected over 11 time points. These samples are assayed for vitamin C, vitamin E, nicotine, several immunoglobulins, and several antioxidant carotenoids. The data are used together with information obtained from each study participant's medical history and dietary/smoking questionnaires to determine whether relationships exist between micronutrient status during pregnancy and lactation and the health and nutritional status of mother and baby.

Population Description and Sampling Plan

A total of 130 women who are in their first trimester of pregnancy are enrolled in the study. Past experience indicates that the racial composition of women who come to the prenatal clinic at our institution is approximately one-third white, one-third black, and one-third Hispanic. This racial composition is maintained during recruitment of smoking and nonsmoking subjects for the study. Only pregnant women who are visibly well nourished and without obvious clinical or medical complications are solicited for study enrollment.

Both cigarette smokers and nonsmokers are matched for age, parity, and gravidity. Because the study design is double-blind, neither the study participants nor the clinicians/nurses know the composition of the supplement/placebo preparations. To accomplish this, a random numbering system separately assigns smoking women and nonsmoking women into the respective study groups.

Analysis Plan

Analysis of variance is used to test whether average levels of vitamin C, vitamin E, or individual carotenoids differ among the different study groups at the different time points. Using standard deviations based on our preliminary work, a 0.05 level of significance and a power of the test of 0.90, a sample of 20 subjects per group will allow us to detect true population mean differences as small as 0.22 mg/dl in vitamin C in maternal serum, 0.49 mg/dl in cord serum, and 0.18 mg/dl in infant serum. With respect to vitamin E, we will be able to detect differences as small as 0.18 mg/dl in maternal serum, 0.08 mg/dl in cord serum, and 0.10 mg/dl in infant serum. If the null hypothesis of equal means is rejected, Dunnett's procedure will be used to compare smoking groups against nonsmokers.

For each study group, repeated measurements of the various analyses over time will be available. These measurements are compared by treatment group (smoker versus nonsmoker, supplement versus placebo) with respect to trends in their effects over time as well as mean levels of response. Analysis of variance for repeated measurements is performed and the appropriate adjustments are made to correct the degrees of freedom for testing various hypotheses about the time factor. If the condition of homoscedasticity of the variance at the times of measurement cannot be met, hypotheses about the time factor will be tested using multivariate methods.

Multiple regression is used to examine the relationship between cord serum, maternal serum, infant serum, and breast milk in smokers and nonsmokers. Multiple regression analyses also are used to estimate the effect of smoking (as indicator, categorical, and continuous variables) on maternal, cord, and infant levels of nutrients and immunoglobulins, and their subsequent effect on gestational age and birthweight, length of gestation, and respiratory symptoms, while controlling for confounding factors such as age, dietary habits, parity, gravidity, alcohol use, drug use, and passive smoking in the home.

SIMULTANEOUS SCREENING FOR HEARING, SPEECH, AND LANGUAGE

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PROJECT NUMBER MCJ-370574

PROJECT PERIOD 01/01/88–09/30/91

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	240,665	261,161	267,545	Denied	Denied
Requested	309,172	292,288	300,951	348,440	368,429

* Indirect included

SUMMARY

Statement of the Problem

The problem of identifying preschool children with disorders of the communication system is an issue that has recently been recognized as a top national educational priority. Beginning in 1991, all States are required to identify preschool children with developmental disabilities, so that early intervention programs might be implemented. The first goal of the U.S. Department of Education's Year 2000 Plan is that all children begin school ready to learn. According to the most recent Carnegie report on education in the United States, a lag in communicative abilities is the most common reason for initially poor adaptation to school. Prevalence estimates and case definitions indicate that disorders of the communication system are the most prevalent of the developmental disabilities.

The American Academy of Pediatrics (AAP) has recently recommended that pediatricians take a role in the newly mandated early identification process by using screening tests to identify children at risk for developmental disabilities. In an earlier policy statement, AAP encouraged pediatricians to make screening for developmental disabilities as routine as vision and hearing screening.

However, there is reason to believe that limitations to such screening in pediatric practice are less related to attitudes that can be changed by encouragement than to practicalities of time constraints. A practice survey has shown that most pediatricians (97 percent) accept the recommendation to screen for developmental disabilities, but 85 percent omit standard screening procedures because they are too time consuming. These pediatricians report that they screen for developmental problems through informal observation of the child during the course of routine examinations. However, even the observations of experienced pediatricians have been found to be unreliable for detection of developmental problems.

Our past research has demonstrated the efficacy of observations of developmental/readiness functioning during the course of a vision acuity screening which was reorganized from a developmental point of view, but not lengthened. This brief test (8 minutes in length) was more predictive of school outcomes than the results of the child's IQ testing. This vision/developmental test illustrates a model of combining a health routine with developmental screening to achieve the American Academy of Pediatrics' goal of making preschool developmental screening as routine as vision and hearing screening by capitalizing on the method of simultaneous screening that pediatricians claim they already perform. This general approach overcomes the obstacles of insufficient time. However, the vision/development screen was not adequate for speech and language screening.

Research Questions or Hypotheses

The ultimate goal of this project is to: (1) Develop a means of screening for speech, language, and hearing problems in a child health setting, using no more time than is ordinarily committed to hearing screening alone; and (2) improve the current hearing screening procedures in order to be more sensitive to a wider range of audiological impairments than is possible by current routine pure tone screening procedures.

The goals of this initial funding phase are to (1) develop a prototype instrument by selection of stimuli through studies of normal children, (2) complete a validation study of the stimuli in normal and hearing impaired children, and (3) collect validation data for children with speech and language impairments. Successful completion of this project will provide a cost- and time-effective system to identify communicative handicaps in pediatric practice.

Study Design and Methods

A large pool of minimally paired monosyllable words (i.e., a target and three foils, which differ by a single consonant) are selected. Professionally photographed pictures of these words are created, following preliminary studies of the optimal visual format and recognition vocabulary of drawn pictures. Artistic renderings of sentence stimuli are also created. Audio recordings of the potential target items are brought to a level of 100 percent recognition by expert listener panels. Earphones were selected following a national survey of expert clinicians and a study of acoustic response characteristics.

A series of psychoacoustic studies is conducted in the sample of preschool children and adults in order to find the stimulus characteristics for which a very small change in stimuli results in the greatest fall-off in performance (i.e., the "knee" of the function). These studies define the parameters for desired type of maskers (babble), preferred intensity level of signal (35 dBHL), signal-noise ratio (+ 5 for identification responses and + 10 for expressive responses), and best mode of presentation of the items (i.e., expression separate from identification). The resulting parameters are then incorporated into the prototype by means of ongoing hardware and software development.

Population Description and Sampling Plan

A total of 123 children and 137 adults participate in the prototype development studies. All of the child subjects are identified as normal by scoring in the normal range on diagnostic tests for speech, language, hearing, and middle ear functioning. Children between the ages of 3 years 6 months and 5 years 5 months complete speech, language, tympanometry, and hearing testing with normal hearing and mild conductive subjects selected. In addition, data are collected on 73 children with speech or language impairments and 197 normal children.

Analysis Plan

In order to obtain preliminary estimates of the potential of the most parsimonious set of items to maximally predict group membership, discriminant function analyses are completed using the subset of items that are significant at the univariate level.

PREDICTION OF OUTCOME OF EARLY INTERVENTION IN FAILURE TO THRIVE

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PROJECT NUMBER MCJ-390557

PROJECT PERIOD 11/01/87–10/31/90

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	91,958	72,014	65,511	n/a	n/a
Requested	91,958	75,525	78,639	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

Nonorganic failure to thrive (NOFTT) is a pediatric problem that occurs frequently, can be reliably detected during infancy, and is associated with a high degree of psychological risk. However, the specific areas of psychological development most vulnerable to the effects of NOFTT and associated risk factors have not been well documented. One of the most salient but, as yet, unanswered questions concerns the processes that affect the long-term socioemotional outcomes of infants with nonorganic failure to thrive. Although physical symptoms and malnutrition associated with NOFTT generally remit with medical treatment, psychological symptoms are identified long past the point of diagnosis and early treatment.

Moreover, research has not yet identified the factors that influence positive versus negative health and psychological outcomes among children with early histories of NOFTT who received pediatric and psychological intervention as infants. For this reason, clinical practitioners do not have an adequate base of knowledge to guide their decisions concerning psychosocial treatment and long-term planning.

This study is designed to address the need for controlled studies of psychological outcome in preschool children with early histories of NOFTT, using a comprehensive assessment approach. Nonorganic failure to thrive occurs among children with a wide range of family, ethnic, and socioeconomic backgrounds.

Research Questions or Hypotheses

The purpose of this study is to conduct a controlled, prospective followup of children with early histories of NOFTT who received early intervention as infants; the study includes a comparison group of physically healthy children from infancy to 48 months of age.

The study has two primary objectives:

1. Comprehensive assessment of the psychological outcomes of a cohort of children ages 42 and 48 months, who were initially hospitalized for NOFTT as young infants and who received time-limited early intervention following hospitalization. The outcome of this group is compared with that of physically healthy children from similar socioeconomic circumstances.
2. Identification of factors that predict the psychological outcomes of preschool children with NOFTT who received comprehensive pediatric and psychosocial intervention as infants.

Specific hypotheses include the following: (1) Children with early histories of NOFTT will demonstrate greater frequencies of psychological symptoms and less adaptive psychological development than physically healthy children from comparable socioeconomic backgrounds; and (2) quality of family functioning will predict behavioral symptoms.

Study Design and Methods

Predictor variables include security of attachment as assessed by the Ainsworth Strange Situation Procedure, and quality of family relationships as assessed by the Family Environment Scale. Outcome measures include (1) psychological competence based on home observation; and (2) experiment-based measures of ego control and ego resiliency, family functioning, family environment, and behavioral symptoms (Child Behavior Checklist); and (3) a measure of problem solving.

The comprehensive outcome assessment uses data gathered from multiple observations, starting at 12 months of age and continuing through 48 months. In addition to the primary or target measure pertaining directly to socioemotional development, children's cognitive development and physical growth are assessed.

Population Description and Sampling Plan

The sample of children with early histories of NOFTT was recruited from six hospitals in the Cleveland area. Children (*N* =48) were between 1 and 9 months of age, met objective criteria for growth deficiency, and had no primary organic or constitutional etiologies for their growth deficiency based on comprehensive pediatric evaluation and physical diagnostic tests. Physically healthy and normally growing children (*N* =47) in the comparison group were recruited from similar health care facilities and geographic locations as the NOFTT sample. This comparison group was added to control for variables known to affect the long-term psychological outcomes of children with NOFTT. These include child characteristics (age, sex, race, birth order, prematurity), maternal characteristics (maternal education and age), and family characteristics (family size, income, and constellation). The majority of the overall sample (*N* =78) came from economically disadvantaged families who receive Aid to Dependent Children. The racially heterogeneous sample included 64 African-American children and 31 white children.

Analysis Plan

Data analysis plans include a description of the populations, analysis of group differences, and multiple regression analyses to describe predictors of psychological functioning.

OTITIS MEDIA IN DAY CARE: EFFECTS ON LANGUAGE/ATTENTION

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PROJECT NUMBER MCJ-420565

PROJECT PERIOD 03/01/88–02/28/93

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	184,322	182,857	210,873	197,277	141,038
Requested	205,098	203,173	213,502	193,330	138,847

* Indirect included

SUMMARY

Statement of the Problem

Otitis media is a very common disease in childhood. Most children have at least one episode of otitis media before the age of 3, and up to one-third of children have chronic problems with this disease. The symptoms of the disease vary, and more than half of the children with otitis media have no symptoms at all, making the disease difficult to detect. Although antibiotic regimens have helped to reduce the acute phase of the disease, there is no completely effective therapy for the fluid that often remains in the middle ear after the acute phase is over. This fluid can last many months after an active infection, and is associated with a mild to moderate hearing loss.

Behavioral scientists have become concerned about this disease not only because it is so frequent but also because the hearing loss that results occurs at a critical time in the development of children, when language and other important social cognitive skills emerge. Many retrospective studies and a few prospective studies have shown a relationship between bouts of otitis media and later language and intellectual deficits. However, all of these studies suffer from design flaws, and none of them examined whether overall illness, independent of otitis media, might be related to developmental problems.

Research Questions or Hypotheses

This study examines three ways in which otitis media may affect concurrent or later development:

1. Is illness in general, or otitis media specifically, related to immediate or later speech/language and attention skills?
2. Does otitis media and its resultant hearing loss differentially affect immediate or later speech/language comprehension and production skills, auditory perception/discrimination, or attentional processes?
3. Does otitis media and its resultant hearing loss affect language in later years indirectly through children's poorer attention to language input, which then affects higher order language processes?

Study Design and Methods

This is a prospective longitudinal study. The project studies infants who attend day care, since infants who attend day care have been estimated to have up to three times the amount of otitis media compared to infants who do not attend day care. Infants are enrolled in the study over a period of 2½ years, entering day care as infants. Most infants are enrolled between 6 and 12 months of age and continue in the study until 48 months of age.

Children's health status is monitored very closely. All children are screened for any kind of illness on a weekly basis by a registered nurse. Any child who is found to be ill with any kind of disease is seen by a physician (in 70 percent of these cases, either immediately after seeing the nurse or the next day). Reliability is then calculated between the nurse and doctor, and, if there are disagreements, a recheck is done. Otitis media is diagnosed by a combination of pneumatic otoscopy and immittance audiometry (tympanometry). Acoustic reflectometry is used when these other two methods are not possible, especially with young infants.

Hearing status is assessed every 3 months as well as periodically, when a child has an episode of otitis media. All testing is done in an audiometric test booth using state-of-the-art equipment. Sound field testing is done with very young infants, until earphones can be used. Behavioral reinforced audiometry is used to determine speech awareness thresholds, speech recognition thresholds, and pure tone testing as the children are developmentally ready.

Children's language development is assessed through standardized tests, such as the Sequenced Inventory of Communication Development at 24 months and the Test of Language Development at 48 months. In addition, videotaped language samples are obtained at 3-month intervals beginning at 12 months until 24 months of age, and at 6-month intervals thereafter.

Attention to language is measured through questionnaires given to parents and teachers, observations of the children in the classrooms, and an experimental procedure in the classroom. This experimental procedure, called Attention to Bookreading, is performed at 6-month intervals when the children are well, when they are sick but do not have otitis media, and when they have otitis media. Not all children can have these sessions at each age level, but a subset can be used at each age level to examine how behavior changes as a function of illness, otitis media, or well status. During this procedure, an experimenter in the classroom reads an interesting picture book to the children during free play, so there are many possible distractions for the child. Another experimenter codes the child's attention and nonattention to the bookreading in 5-second blocks (a control procedure was used to rule out visual attention as the primary reason for attention to the book). Other measures are obtained from family interviews at yearly intervals and from teacher questionnaires.

Population Description and Sampling Plan

The 90 children in the study come from three day care centers that serve infants and young children. All children have English as their primary language. The day care centers serve an overwhelmingly middle class population. All parents have at least a high school degree, all but one child comes from a two-parent family, and family income is well above the national average. Thus, based on demographic variables, these children are not at risk for developmental problems.

More than 90 percent of all parents who were contacted about the study agreed to participate. In fact, some families who wanted to participate had to be turned down. Projections are that between 25 and 35 percent of the sample will be lost over the course of the study.

Analysis Plan

Initial analyses employ repeated measures, multivariate analyses of variance, and regression. Growth curve analyses are also done. The attention hypothesis is tested with the data at 12 and 18 months of age. Using the children as their own controls, well episodes are contrasted with otitis media episodes to determine whether children with chronic otitis media differ from those who do not have chronic otitis media.

BEHAVIORAL INTERVENTION WITH IUGR INFANTS

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PROJECT NUMBER MCJ-440569

PROJECT PERIOD 07/01/88–06/30/91

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	152,029	214,966	194,760	n/a	n/a
Requested	201,501	202,093	211,636	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

The purposes of this study are to: (1) Examine the effectiveness of a parent-infant based behavioral intervention during the neonatal period to prevent or ameliorate the negative consequences of intrauterine growth retardation (IUGR) on maternal-child sensitivity and infant physical growth, caloric intake, cognitive development, and language development; and (2) examine the mediating effects of cultural context and risk status on the effectiveness of intervention with IUGR infants.

This study is based on a theoretical model of development in which the impact of an early insult such as intrauterine growth retardation on the developing infant is a function, in part, of the characteristics of the caregiving environment. The intervention is expected to affect outcomes directly by improving caloric intake and indirectly by improving mother-infant interactions.

Research Questions or Hypotheses

The study addresses the following hypotheses:

1. A parent-infant based intervention will improve physical growth and developmental outcome in IUGR infants. The intervention will affect outcome through two pathways—by improving caloric intake and by improving mother-infant interaction.
   a. IUGR infants without intervention will have the highest nonoptimal interactive scores during feeding in the neonatal period and at 4 months of age;

b. IUGR infants without intervention will have the lowest caloric intake during the first 4 months of life;
c. IUGR infants without intervention will have the slowest physical growth during the first 18 months of life;
d. IUGR infants without intervention will have the lowest maternal sensitivity scores at 8 months of age;
e. IUGR infants without intervention will have the lowest Sequenced Inventory of Communication Development-Revised Edition communication scores, and the lowest scores on the Mental Development Index, Psychomotor Development Index, and Kohen-Raz subscales of the Bayley Scales of Infant Development at 12 and 18 months; and
f. IUGR infants with higher caloric intake and higher maternal sensitivity scores will have higher developmental status scores.

2. The impact of the intervention will be mediated by environmental risk and cultural factors.

Study Design and Methods

This study is a randomized clinical control trial of an intervention in which 3 groups are compared at 2 sites, with 35 infants in each of the 3 conditions: IUGR with intervention, IUGR with no intervention, and non-IUGR with no intervention. IUGR infants and their mothers are randomly assigned to the intervention or nonintervention conditions. They are matched to a control group of full-term, non-IUGR infants on the basis of parity, family socioeconomic status, sex, and total neonatal score. The characteristics of subjects who discontinue participation in the study are carefully monitored to rule out selective bias, as are the characteristics of potential subjects who decline intervention.

The intervention, which is performed at three time periods (birth, 2 weeks postpartum, and 4 weeks postpartum), consists of reviewing with the mother the first 15 minutes of a videotaped feeding sequence. Mothers are trained to carefully observe specified dimensions of the infant's state and the mother's and infant's behavior, with the aim of increasing the mother's contingent and sensitive responses to her infant. To control for the effects of extra contact, the research assistants meet with the mothers who are not assigned to the intervention and discuss topics such as birth experiences. Assessments are conducted at seven time periods over the first 18 months of life (birth, 2 weeks, 4 weeks, and 4, 8, 12, and 18 months), and are conducted both in homes and in a laboratory.

Caloric intake, feeding interactions, physical growth, and maternal-infant sensitivity are assessed during the infants' first year, using standardized measures and other measures developed by the investigator which have proved useful in other investigations and which have acceptable reliability. Maternal sensitivity is assessed using the Home Observation for Measurement of the Environment inventory. Later assessments focus on standardized assessments of the infants' developmental status (cognitive development and communicative competence), using the Bayley Scales of Infant Development and the

Sequenced Inventory of Communication Development-Revised. Physical growth is assessed using multiple methods.

To assess cultural differences in childrearing attitudes that may mediate the effects of the intervention and IUGR, the Concepts of Development Questionnaire is also administered to the mothers. Data pertaining to a variety of factors that constitute environmental risk (e.g., family size, stressful life events, and social support) are also assessed.

Population Description and Sampling Plan

White non-Hispanic and Hispanic subjects for this study are recruited from two tertiary care facilities in Providence, Rhode Island, and San Juan, Puerto Rico, respectively. The sample consists of 210 full-term infants (140 IUGR infants and their mothers, and 70 control infants and their mothers). Mothers with a significant history of substance abuse, eating disorders, or severe heart disease are excluded. Intrauterine growth retardation is defined on the basis of birthweight and a ponderal index below the 10th percentile, without any other fetal complications; the latter is assessed on the basis of clinical examination. These criteria are adopted to reduce the heterogeneity of the sample.

Analysis Plan

The data analysis strategy is to first analyze the effects of the intervention separately for each site on the different dependent variables, using repeated measures analyses of variance (with time as the repeated measure). Hierarchical multiple regression analysis is used to test the relative effectiveness of caloric intake versus maternal sensitivity in determining developmental outcome. Then, the effects of the proposed mediators of the impact of the intervention (e.g., environmental risk, cultural code, and etiology of IUGR) are determined, either by repeating the first set of analyses using site as an independent variable and risk factors as a covariate, or by using hierarchical regression.

ACCULTURATION, PSYCHOSOCIAL PREDICTORS, AND BREASTFEEDING

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PROJECT NUMBER MCJ-480555

PROJECT PERIOD 04/01/87–03/31/90

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	254,598	320,565	235,084	n/a	n/a
Requested	254,534	380,585	276,607	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

The incidence of breastfeeding in the United States has been low compared to the rest of the world and has slowly declined from a peak of 62 percent in 1984 to about 52 percent in 1990. Hispanics and black Americans have breastfed at particularly low rates. In order to ultimately increase the incidence and maintenance of breastfeeding, we are investigating the reasons that adaptation to U.S. culture reduces breastfeeding rates in the target population of Brownsville, a city on the border between Texas and Mexico. This population is primarily Hispanic and of low socioeconomic status. A higher breastfeeding rate in this population would engender both health and economic advantages for these mothers and infants.

Research Questions or Hypotheses

This project addresses the hypothesis that acculturation to the United States is associated with a reduction in the rate of breastfeeding in a population of mothers originally from Mexico. Furthermore, a number of psychosocial variables will reflect this acculturation and will be associated with the breastfeeding decision. These variables include social support/influence, maternal expectations, maternal behavioral capability, maternal self-efficacy, environmental constraints, and paternal expectations.

Study Design and Methods

This study consists of a structured interview developed to contain instruments to measure each of the psychosocial variables as well as items to assess health, demographics, and acculturation. The eligible population includes all mothers giving birth in Brownsville, Texas, during the 15 months of the study. A pilot study of 213 mothers was conducted to refine the instruments and develop recruitment techniques. The mothers are interviewed prenatally (in the last trimester), natally (in the first 10 days after delivery), and postnatally (approximately 1 month after delivery). The husband or male partner is interviewed during the prenatal period. Successful initiation of breastfeeding is defined as any breastfeeding at the time of the postnatal interview.

Population Description and Sampling Plan

The population was recruited from all mothers in Brownsville, Texas, who gave birth during the 15-month sampling period. Approximately 3,300 women gave birth during this period; 37.2 percent were contacted and 27.4 percent ($N = 906$) were recruited to participate. The participating mothers reflect the distribution among the Brownsville population (as reported by the city health department) in terms of the four possible birthing sites: Two private hospitals (35 percent and 24 percent, respectively), maternity center (13 percent), and lay midwife *partera* (25 percent) . The birthplaces of the subjects' previous children had a similar distribution: Two private hospitals (31 percent and 23 percent, respectively), maternity center (18 percent), and lay midwife (24 percent).

Analysis Plan

Frequencies for each variable are calculated and chi-square analyses are used to survey for associations between breastfeeding initiation and the other variables. The acculturation, social support, maternal expectations, and behavioral capability scales are investigated for internal variables by use of factor analysis. Composite variables are calculated for each of these items based upon the factor analysis. Further associations among these variables are calculated using Pearson's and Spearman's regressions as appropriate. Predictive models for breastfeeding are calculated using linear logistic regression.

UTERINE ACTIVITY PATTERNS: DEFINITION WITH HOME MONITOR

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PROJECT NUMBER MCJ-480561

PROJECT PERIOD 12/01/87–11/30/89

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	201,745	191,640	n/a	n/a	n/a
Requested	212,908	201,290	n/a	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

Preterm birth, defined as any delivery occurring prior to the 37th complete week of pregnancy, occurs in approximately 8–10 percent of births nationwide. These births, in turn, account for 75 percent of all perinatal morbidity and mortality. Despite the availability and use of tocolytic agents, the incidence of preterm delivery in this country and others has remained unchanged over the past 20 years. New attention has been directed to programs that focus on early detection of preterm labor, through patient education, frequent patient-caretaker interaction, and in some cases, the use of an ambulatory uterine activity monitor. It has been proposed that home ambulatory uterine activity monitoring might be a very effective means by which (1) the patient at risk for preterm delivery could be identified and prophylactic measures against subsequent preterm labor could be employed, and (2) preterm labor could be detected early and treatment initiated without delay.

Research Questions or Hypotheses

This research is aimed at establishing normative data of uterine activity in normal pregnant women throughout the last 20 weeks of gestation. The underlying hypothesis (not specifically addressed in this study) is that deviations from normative uterine activity may be useful in the prediction and/or early detection of preterm labor. This descriptive study is designed to determine whether there is a measurable increase in frequency, duration, or amplitude of uterine contractions in normal singleton pregnancies and whether the change is gradual, continuous, or discontinuous. In addition, the study will determine whether uterine activity changes as a function of parity, physical activity, or emotional state.

Study Design and Methods

The study is conducted at three sites: The University of Texas Medical School at Houston, the University of California at San Diego, and Ohio State University. The University of Texas School of Public Health, Epidemiology and Biometry Section, assists in data management and analysis.

Patients who agreed to enter the study were requested to wear a specially designed external tocodynamometer, which can store uterine activity for two complete 24-hour periods, beginning at 20–24 weeks, twice a week for the remainder of their pregnancy. The stored information is downloaded at a convenient time. At this time, an hourly log of 24-hour physical activity and 24-hour visual emotional state is reviewed by the nurse and then forwarded by mail for data input. Uterine activity is transmitted by telecommunication into a microprocessor onto hard disk storage and backed up. Each contraction is recorded by date, minute of the day, duration, and amplitude. The physical activity log is coded by six levels of physical activity.

Final outcome of gestation is determined for each participant. Patients with preterm delivery, infectious processes accompanying early labor, anomalous births, polyhydramnios, fetal growth restriction, and maternal medical disease are excluded from the normative data, along with patients who do not complete the study.

Population Description and Sampling Plan

As indicated above, the study is performed at three clinical centers. Recruitment signs were placed in various clinics, and individuals were screened at their first prenatal visit. The only inducement offered was a waiver of physician fees above any third party coverage.

Patients were approached for recruitment and informed consent if they were 18–35 years of age for primigravida and 18–40 years of age for multigravida, and if they did not have the following exclusionary data: History of midtrimester loss, history of more than two abortions, a previous preterm labor or birth, a multiple gestation, a previous cone biopsy, a known uterine anomaly, chronic maternal medical disease, or bleeding after 12 weeks of pregnancy.

A total of 4,509 patients were screened; of this number, 168 patients enrolled in the study, and 117 patients completed the study. A total of 109 patients were considered to have deliveries at term that were uncomplicated by the definitions used. The study included 51 primigravid and 58 multigravid patients for the final analysis.

Calculations performed at the onset of the study indicated that a sample size of 95 would be sufficient to compare uterine activity across gestational ages, define diurnal rhythms, and compare uterine activity according to parity.

Analysis Plan

Differences in continuous variables are assessed with Student's *t* tests and analysis of variance where appropriate. Differences in ordinal or categorical variables are tested using the chi-square statistic with the Yates correction for continuity. Correlations between variables are assessed using linear regression techniques.

SICKLE CELL ANEMIA:
DNA FOR NEWBORN SCREENING FOLLOWUP

GRANTEE Baylor College of Medicine

INVESTIGATOR

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PROJECT NUMBER MCJ-480566

PROJECT PERIOD 04/01/88–03/31/90

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	73,690	Denied	Denied	n/a	n/a
Requested	88,442	91,280	96,749	n/a	n/a

* Indirect included

SUMMARY

Statement of the Problem

This research project addresses the problem of followup to newborn screening for sickle cell anemia using direct DNA confirmatory diagnosis from the initial newborn filter paper blotter. Neonatal hemoglobinopathy screening requires sensitive electrophoretic determination of the abnormal beta-globin. Newborns with a very low proportion of the adult hemoglobin represented by the sickle (S) beta-globin, and with a high proportion of fetal hemoglobin, may have an equivocal diagnosis of carrier (AS) versus homozygous affected (SS) status after screening by protein electrophoresis. This confusion can frequently be resolved by confirmatory followup electrophoresis using a liquid blood specimen, although even this may not resolve the issue for a period of 2–4 months, until the adult beta-globin gene is turned on sufficiently.

The major problem that results from equivocal or delayed diagnosis of sickle cell anemia has to do with antibiotic prophylaxis in the patient with SS disease. This therapy may be initiated later than it should be, it may not be started at all, or the family may not continue the antibiotic regimen appropriately. All of these actions place the infant at risk for life-threatening infection, particularly from overwhelming infection due to *Streptococcus pneumoniae*. Infection can occur at 4 months of age and is most likely during the first 3 years of life. The fatality rate in patients with SS disease can be as high as 30 percent with this infection.

Research Questions or Hypotheses

This project evaluates a technical innovation, the extraction of DNA from the dried blood spot from the newborn screening blotter and amplification of the beta-globin gene sequence to allow a rapid and specific followup DNA test for SS disease from the newborn screening blotter.

Study Design and Methods

Specimens are sent from the State newborn screening laboratory at the Texas Department of Health to the DNA followup laboratory at Baylor College of Medicine. These samples are single, 1/2-inch circles cut from neonatal specimen blotters after all routine screening tests have been performed. The identity and electrophoretic results of these are unknown to all of the personnel in the DNA laboratory. The results from the State screening laboratory are revealed only after the DNA genotype has been determined.

A 1/2-inch semicircle is cut from each specimen circle of dried blood using stainless steel scissors which are routinely washed in 0.3N HCl for 10 minutes between samples in order to depurinate DNA and prevent cross-contamination of specimens. Each semicircle represents the dried equivalent of approximately 25 μl of whole blood. The microextraction procedure is similar to that reported previously, with the exception that the proteinase K digestion is extended from 2 hours to approximately 16 hours (overnight) in order to improve DNA yield. The procedure includes methanol fixation, sodium dodecyl sulfate (SDS) and proteinase K treatment, phenol extraction (3x), chloroform-isopropyl alcohol extraction (2x), ethanol precipitation and drying the precipitated DNA. After dissolving the DNA in 100 μl TE (10 mM Tris HCl and 1 mM EDTA, pH 8.0), the quality is evaluated and the concentration is estimated by electrophoresis of a 10 μl aliquot with standards of known concentration on a 1 percent ME agarose gel which is stained with ethidium bromide. The DNA median yield is 1,500 ng/semicircle (range 900–2,000 ng/semicircle) or approximately 60 ng/μl dried equivalent of whole blood (range 36–80 ng/μl).

An aliquot of DNA (generally 200–300 ng or 10–20 percent of the microextracted material) is taken for amplification using 2.5 u Thermus aquaticus (Taq) polymerase (Cetus), and reaction buffer and other components as previously described, for a reaction volume of 100 μl. A DNA Thermal Cycler (Perkin Elmer Cetus) is used for 30 cycles of amplification: Denaturation 94°C for 0.5 minutes, annealing 55°C for 0.5 minutes and extension 72°C for 1.0 minute. Two primers flanking a 299 base pair (bp) genomic region containing the sickle cell mutation are used: PC0325 and PMC1110 (5′-CTCAAAGAACCTCTGGGTCC-3′).

Subsequently, we adapted a method from Schwartz et al and previous work on boiling of specimens from our group, which avoided the need for manual microextraction. Aliquots measuring approximately 4 mm × 4 mm (representing the dried equivalent of approximately 8 μl whole blood) are cut from each dried blood specimen and placed in 1.5 ml microcentrifuge tubes to which the complete amplification cocktail including primers, and in some cases Taq polymerase, are added as described above. These microfuge tubes are then placed in the automated thermal cycler programmed with an initial 15-minute step at 95°C followed by 30 cycles of amplification described above, modified to increase the 94°C denaturation step from 0.5 to 1.0 minute. If Taq polymerase has not been added prior to the initial 15-minute cycle, it is added after this step and before the 30 cycle amplification program is initiated. Following amplification, the tubes are centrifuged, the supernatants removed and aliquoted for analysis.

Four detection methods are used to analyze the amplified products in the blinded assessment of samples from the State screening laboratory. Each method uses 10–20 μl of the 100 μl PCR reaction volume. Two of these methods are based on dot-blot or slot-blot hybridizations of amplified DNA with allele-specific oligonucleotide (ASO) probes (p19A and p19S), either labeled with radioactive phosphorus or horseradish peroxidase.

The third approach involves direct digestion of the PCR amplified product with DdeI and separation of the restriction fragments by agarose gel electrophoresis in a method adapted from Kazazian. The fourth method utilizes Southern blotting and hybridization with radioactive phosphorous-labeled ASOs.

Products of direct amplification reactions are analyzed for the A, S, C, and E alleles using dot-blot or slot-blot hybridizations with radiolabeled ASO probes. The A, S, and C ASOs are 19-mers previously described (p19A, p19S, and p19C), and the E ASO is a 20-mer which we have designated p20E (5'-AAGTTGGTGGTAAGGCCCTG-3').

Microextracted DNA is amplified using oligonucleotide primers flanking the mutation site. Fluorescent DNA sequence primers are prepared and fluorescent DNA sequencing is carried out using the ABI Automated Sequencer.

Population Description and Sampling Plan

The State Newborn Screening Laboratory sends remains of each newborn screening specimen that had a hemoglobin electrophoresis diagnosis of sickle cell disease carrier or affected. These specimen portions are sent after the State Newborn Screening Laboratory has completed all of their testing. If these specimen remains had not been sent to our laboratory, they would have been discarded.

Analysis Plan

Each specimen received in our laboratory is tested to provide a DNA diagnosis two or more times. The first two tests of each specimen are compared, and percent agreement is determined. This is accomplished for all of the specimens and also for each diagnostic category as determined by the State Newborn Screening Laboratory. These data provide information as to the reliability of our DNA diagnosis.

The DNA diagnosis from our laboratory is compared with the hemoglobin electrophoresis diagnosis from the State Newborn Screening Laboratory for each specimen. Percent agreement among these two laboratories is computed. We determine this overall for all of the specimens and specifically for each diagnostic category made by the State Newborn Screening Laboratory. These data provide information as to the validity of our DNA diagnosis.

LISTENING PARTNERS: PSYCHOSOCIAL COMPETENCE AND PREVENTION

GRANTEE University of Vermont

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PROJECT NUMBER MCJ-500541

PROJECT PERIOD 10/01/86–09/30/90

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	192,237	233,161	196,089	100,320	n/a
Requested	211,085	229,791	135,071	130,165	n/a

* Indirect included

SUMMARY

Statement of the Problem

Many impoverished, isolated, rural mothers raised in socially isolated, hierarchically structured, and relatively nonverbal households have little opportunity to develop a sense of the power of their own minds and voices. With little reliance on their minds or words for problem solving and communication, these women are more likely to turn to power-oriented techniques for influencing their own children (much as their parents did with them). The developmental position of these women is likely to be associated with authoritarian childrearing strategies and limited appreciation of their children's social and cognitive capacities. Unable to feel the power of their own minds, many of these mothers do not imagine and draw out such capacities in their children. Failing to think and talk things through with their children, the mothers often do not explain what they know nor do they ask their children questions that might help the children generate their own ideas, explanations, and choices. Literature has documented that these parenting practices and attitudes are linked to delays and/or limitations in children's thinking and learning skills, self-concept and self-esteem, and social competence and peer acceptance, as well as increased behavior problems in children. Moreover, the children are left with many of the thinking and parenting strategies of their parents, thus perpetuating these patterns through subsequent generations.

The Listening Partners Program examines the intellectual and social development of white mothers who have children under age 7, and who are impoverished, isolated, and living in rural Vermont. The program investigates the relationship of these characteristics to parenting strategies and concepts of these women, and the development of their preschool-age children. Moreover, the program implements and evaluates a preventive intervention designed to promote women's intellectual and ethical development, which are believed to support the development of constructive parenting concepts and strategies and, in turn, the development of healthy children.

Research Questions or Hypotheses

The specific research objectives of the study are to:

1. Examine the interrelationships among (a) mothers' intellectual reasoning, (b) mothers' ethical reasoning, (c) maternal self-concept, (d) maternal self-esteem, (e) mothers' parental communication strategies and conceptualizations of the child, (f) mothers' social support networks, (g) mother-child interaction, (h) children's perceived competence, and (i) children's interpersonal cognitive problem-solving skills. While there are substantial theoretical bases for linking these components with one another, relevant empirical evidence is limited. Further demonstration and clarification of the interrelatedness of these characteristics can contribute to a fuller understanding of the nature and functioning of each characteristic, improved design and selection of program evaluation and developmental assessment tools, and development of more effective promotive and preventive intervention strategies.
2. Gather systematic data on impoverished rural mothers and their interactions with their young children. Limited systematic data are available on the psychological development and parent-child interactions of this population; the vast majority of available research has focused on urban and suburban populations.
3. Develop a cost-effective promotive intervention for mothers and young children that is particularly sensitive, both on psychological and practical grounds, to the needs of the rural poor.
4. Determine the effects of the Listening Partners intervention on (a) the development of the mothers' intellectual and ethical reasoning, (b) maternal self-concept and self-esteem, (c) parental communication strategies and conceptualizations of the child, (d) maternal social support networks, (e) mother-child interaction, and (f) children's perceived competence and interpersonal cognitive problem-solving skills.

Study Design and Methods

Two cohorts of isolated, rural, impoverished mothers of preschool-age children were recruited to the project ($N = 120$; 59 experimentals and 61 controls). During an 8-month period, a total of 34 weekly intervention sessions are implemented with the experimental group. Within each cohort, three groups of approximately 10 women each meet for approximately 2½ hours per week, with different pairs of project staff members acting as group facilitators for each group. Child care is provided for the participants' preschool-age children (target and nontarget) by 3–5 community lay women. The intervention centers around the concept of "gaining a voice," the metaphor used recurrently by the women for growth of mind. We hope to support participants in becoming aware of the power of their own minds, and in becoming good friends and good interviewers (i.e., drawing out each other's voices and thoughts as they learn to talk and think things through together), and thus becoming better problem solvers. Not only do we want to give women the experience of participating in an ongoing, high quality dialogue with peers, but we also hope that the women themselves will go on to create such experiences for their friends and families, especially their children.

The intervention sessions concentrate on a set of closely related activities: (1) Reflective dialogues, active listening, storytelling; (2) cooperative problem solving; (3) free-talking journals, (4) disseminating personal stories, and (5) self-evaluation and metathinking.

Each of the 120 project participants and their children complete assessments at 3 points in time: Preintervention, postintervention (approximately 9 months later), and followup (approximately 9 months following the postintervention assessment). Mothers are engaged in 90-minute to 2½ hour interviews that include a self description; the Ways of Knowing assessment of epistemological perspective; the hypothetical moral dilemma; and the Parent-Child Communication Beliefs Interview. They also complete the Rosenberg self-esteem measure and the Family Social Support Scale. Study children ages 4.0–6.8 years complete the Preschool Interpersonal Problem Solving Test and Harter and Pike's Pictoral Preschool Competence Scale. In all families, mother-child interaction is videotaped at three points: A 10-minute free-play session, two 5-minute semistructured teaching tasks, and a 5-minute cleanup period.

A minimum of .80 interrater coder agreement was reached for all measures. Coders are blind to participants' experimental groups as well as to their scores on other measures.

Population Description and Sampling Plan

Two cohorts of 60 women ($N = 120$) were recruited from the same two contiguous and similar rural, impoverished, sparsely populated counties in northeastern Vermont. Given the nature of this rural population, all participants are white. Mothers are eligible to participate in the project if they meet the following criteria: (1) Age between 17 and 34 years, (2) at least one child under age 7, (3) living below the Federal poverty level, (4) living in social/rural isolation, (5) family identified by one or more referring agencies as having little family support and as being at risk for abuse or neglect of the children or under unusual stress, and (6) lack of involvement in support and self-help groups. For the purposes of the assessments, the project identifies a study child in each family (the child under age 7 and closest to age 4). This group includes 51 girls and 69 boys who range in age from 0.2 to 6.8 years at the time of preintervention assessments.

Names of potential project participants were solicited from social service and mental health agencies and professionals in the locale. We encouraged referrals of families who had refused participation in other community services. Experimental group was assigned by county of residence, given the likelihood that information regarding the intervention would spread among members of the community.

Potential participants were told that we were interested in learning more about the lives of rural women and the experience of raising children in rural isolation, and that we wanted to disseminate this story. They were also told that some of the women in the project would have the opportunity to participate in groups designed to help women break through social isolation, gain a voice, feel the power of their minds, and help participants assist their children in talking and thinking through their problems. They were also informed that they would be compensated $15 at each of three points in time for completing a series of interviews and scales that would require several hours of their time at each sitting.

Analysis Plan

A variety of quantitative statistical analyses are used to examine the following: Interrater reliability among data coders; characteristics of the sample at preintervention; preintervention comparisons of experimental and control groups (chi-square analyses and *t* tests); attrition from the intervention; preintervention characteristics of experimental women who attended intervention group sessions with differential regularity (*t* tests); predictors of attendance at intervention sessions (regression analyses); preintervention comparisons of those who actually attended the intervention versus controls (*t* tests); relationships among preintervention measures (Pearson product-moment correlations, *t* tests, analyses of variance, and multivariate analyses of variance); change from preintervention to postintervention to 9-month followup (multivariate analyses of variance, chi-square analyses); and maternal predictors of epistemological change among both experimental participants and controls (regression analyses).

EPILEPSY IN PREGNANCY: DEVELOPMENTAL FOLLOWUP OF INFANTS

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PROJECT NUMBER	MCJ-530552
PROJECT PERIOD	04/01/87–03/31/90

COSTS*	Year 1	Year 2	Year 3	Year 4	Year 5
Awarded	103,036	109,300	Denied	Denied	Denied
Requested	103,035	108,177	117,638	125,912	130,749

* Indirect included

SUMMARY

Statement of the Problem

Despite decades of concern for the children of epileptic mothers who are exposed in utero both to possible adverse effects of antiepileptic drugs (AEDs) and to the biological concomitants of maternal seizures, research efforts to date are incomplete and controversial. There have been descriptions in the medical literature of patterns of malformations attributed to in utero exposure to antiepileptic drugs, but we still cannot predict which pregnancies are most at risk for adverse outcome. In addition, there have not been many studies of the developmental outcome of these children, and those studies that have been done generally lack adequate controls for parental intelligence, anticonvulsant exposure, and maternal seizure frequency.

Research Questions or Hypotheses

The purpose of this study is to: (1) Examine the outcome of infants exposed in utero to antiepileptic drugs and/or to maternal seizures, and to compare their outcome to that of a group of infants without such exposure; and (2) look for correlates in pregnancy that may predict adverse outcome.

Study Design and Methods

Both groups of children (exposed and nonexposed) are seen at 8 weeks of age by the study pediatrician for a detailed dysmorphology exam. They are seen again at 12 and 24 months of age for a pediatric exam, health history, and administration of the Bayley Scales of Infant Development by a psychometrist. Audiology by visually reinforced audiometry is done at 12 months. Their last visit is at 36 months of age, when they again see the pediatrician for a health history, physical exam, and detailed dysmorphology exam. At this visit, the psychometrist administers the Stanford-Binet Intelligence Scale: Fourth Edition, the motor scale of the Revised Vineland Adaptive Behavior Scales, and a language sample for computing mean length of utterance. The psychometrist also administers the Peabody Picture Vocabulary Test, Form M, to both mother and child.

All examiners (pediatrician, audiologist, and psychometrist) are blind as to whether the children are in the exposed or nonexposed group. However, another physician is available to talk with parents who have specific questions about drug exposure.

Population Description and Sampling Plan

Pregnant women with epilepsy were recruited for this study from a study of epilepsy in pregnancy conducted by the principal investigator at the Epilepsy Center at the University of Washington. As part of this study, the type and frequency of women's seizures and their drug doses and levels were followed closely. The control group of women without epilepsy or other chronic medical conditions was recruited from the prenatal clinic of the University of Washington Hospital. The case and control groups are matched for age, race, and parity. The control group tends to have more years of education, but the difference is not statistically significant.

We originally planned to recruit 147 women in each group, for a total of 294 children in the study. However, the principal investigator relocated in 1987 and funding was terminated for the study at the Epilepsy Center at the University of Washington. At that time, we stopped recruiting new cases and controls for the followup study, leaving us with a total of 56 case and 51 control children.

Analysis Plan

Descriptive measures of growth, language, and motor development are obtained for both the cases and controls. For growth measures (height, weight, and occipital frontal circumference), a two-sample t test or Wilcoxon's rank sum test is carried out to determine whether there is any significant difference between the two groups. Differences in incidence of abnormal growth or motor development are assessed using chi-squared tests.

Although mothers are chosen to assure comparability on factors such as maternal age, differences between the groups can occur in other characteristics, such as method of delivery. Where such differences occur, analysis of covariance or Mantel-Haenszel's method for combining 2 × 2 tables is used to determine whether these factors might explain the observed differences.

As differences between the two groups are established, multiple regression techniques are used to determine whether variability in such factors as maternal AED levels and/or maternal seizure frequency during pregnancy correlate with the outcome variables for the exposed group.

The frequency of outcome measures is compared between the two groups, using t tests or chi-squared tests of statistical significance. In addition, correlations are sought between maternal seizure frequency and maternal AED use with certain pregnancy outcomes, selected parental factors, and selected child outcomes.

INDEXES

Grantee Index

Albert Einstein College of Medicine 81
American Sudden Infant Death Syndrome Institute 163
Baylor College of Medicine 240
The Better Babies Project, Inc. 153
Boston Children's Hospital 183
Boston City Hospital 186
California Pacific Medical Center 146
Case Western Reserve University 106, 227
Children's Hospital 35
Children's National Medical Center 160
Columbia University 87
Dartmouth College 55
Duke University Medical Center 224
Gallaudet University 157
Iowa State University 169
Johns Hopkins University 25, 31, 72, 176
Massachusetts General Hospital 192
Medical and Health Research Association of New York City, Inc. 203
Our Lady of Mercy Medical Center 220
Pennsylvania State University 230
Philadelphia Child Guidance Center 110
Research Foundation for Mental Hygiene, Inc. 77, 206
San Diego State University 3, 132
Stanford University School of Medicine 129
Trustees of Boston University 188
Trustees of Health and Hospitals of the City of Boston 40
Tulane University School of Medicine 173
University of California at San Francisco 136, 140, 143, 149
University of Illinois at Chicago 166
University of Iowa 9
University of Kentucky 13
University of Louisville Research Foundation 20
University of Maryland School of Medicine 179
University of Massachusetts Medical School 195
University of Medicine and Dentistry of New Jersey 61
University of New Mexico School of Medicine 66
University of North Carolina at Chapel Hill 91, 96, 100
University of Rochester Medical Center 215
University of Rochester School of Medicine and Dentistry 211
University of Texas Health Science Center at Houston 238
University of Texas Medical Branch at Galveston 236
University of Vermont 243

University of Washington 116, 121, 247
Wayne State University 45, 50, 199
Women and Infants Hospital of Rhode Island 233

Project Index

A Multidimensional Health Status Index for Infants 211
A Parent-Focused Intervention to Reduce Pain During Procedures 40
A Self-Management Educational Program for Severely Asthmatic Children 66
Acculturation, Psychosocial Predictors, and Breastfeeding 236
Adolescent Mothering and Preschool Behavior Problems 116
An Educational Behavioral Program for PKU 166
Behavioral and Familial Predictors of Injuries in Children 31
Behavioral Intervention with IUGR Infants 233
Body Composition in Pregnant Women 87
Coordinated Care and Case Management for Children with Special Health Needs 192
Determinants of Adverse Outcome Among Toddlers of Adolescent Mothers 206
Drowning Prevention Through Swimming Lessons 121
Early Intervention Collaborative Study: Preschool Phase 195
Effectiveness of an Urban Low Birthweight Intervention 153
Effects at Age Five of An Intervention Program for Low Birthweight Infants 81
Epilepsy in Pregnancy: Developmental Followup of Infants 247
Evaluation of the Guidelines for Maternal Transport 25
Evaluation of the Medi-Cal Comprehensive Perinatal Services 149
Fecal Coliforms and the Risk of Diarrhea in Child Care Centers 100
Feeding Method and Fat Tolerance in Very Low Birthweight Neonates 50
Health and Nutrition of U.S. Hispanic Children 129
High-Tech Home Care for Children with Chronic Health Conditions 13
Home Intervention for Infants with Failure to Thrive 179
Identification of Risk for SIDS: Subsequent Siblings 163
Improved Prenatal Detection of the Fragile X Syndrome 77
Improving Memory in EMR Children 199
Infants of Depressed Adolescent Mothers 186
Interaction and Support: Mothers and Deaf Infants 157
Intravenous Antibiotic Therapy in Cystic Fibrosis: Home Versus Hospital 173
Iron Absorption by Infants 9
Laboratory Evaluation of Jaundiced Newborns: A Reevaluation 143
Listening Partners: Psychosocial Competence and Prevention 243
Maternal Pesticide Exposure and Pregnancy Outcome 132
Maternal Smoking and Vitamin/Antioxidant Status 220
Nature, Origins, and Consequences of Conceptions of Parenting 169
Otitis Media in Children and Later Language and Learning 96
Otitis Media in Day Care: Effects on Language/Attention 230
Outcome Evaluation of A Pediatric Health Care Model 203
Perinatal Risks and Outcomes Among Low-Income Immigrants 3
Physiologic Risk Assessments to Predict Preterm Birth 146
Preconceptional Vitamin Use and Neural Tube Defects 188
Predicting Preschool Function from Contingency Intervention 61

Predicting Teenage Pregnancy 45
Prediction of Outcome of Early Intervention in Failure to Thrive 227
Psychosocial Sequelae of Bronchopulmonary Dysplasia and VLBW 106
Reducing the Nation's Pediatric Intensive Care Mortality 160
Risk Detection Using Observations of Interaction 91
Risk-Taking Behavior in Adolescents: Impact of Puberty 140
Sickle Cell Anemia: DNA for Newborn Screening Followup 240
Simultaneous Screening for Hearing, Speech, and Language 224
Single Parents and Early Intervention Programs 110
Smoking Cessation/Relapse Prevention in Low-Income Mothers 176
Spouse Abuse and Pregnancy Outcomes: A Prediction Study 20
State Census of Technology-Dependent Children 35
Study of Home Visitation for Mothers and Children 215
Study of Psychosocial Factors in Maternal Phenylketonuria 183
Survey of Chronically Ill Children's Use of Time Out of School 136
Use of High Calcium Infant Formula to Prevent Plumbism 55
Uterine Activity Patterns: Definition with Home Monitor 238
Young Adult Users of Services for Children with Special Health Care Needs 72